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Policy

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

Change of Address

Please forward changes of address for the News Letter to Editor: Bureau of Medicine and Surgery, Department of the Navy, Washington, D.C. 20390 (Code 18), giving full name, rank, corps, old and new addresses, and zip code.

FRONT COVER: AEROSPACE CREW EQUIPMENT DEPARTMENT. This research agency was founded in January 1942, has twice been renamed, and is now administratively part of the Naval Air Development Center at Johnsville, Pa., although physically located in Philadelphia. Its mission is to conduct aerospace medical research, especially in personnel protection, support and survival, and it has developed over the years varied types of equipment for air crew protection. Recently ACED's scientific staff has studied metabolic measurements, pulmonary function changes in artificial atmospheres, and the effects of impact acceleration. It has developed a ventilated skin diver's wet suit, a stethescope for use in high-noise levels, and an improved life preserver and survival vest. A program has been initiated to adapt the skin diver's wet suit for use in certain cold weather sea survival situations. The one-piece suit consists of cellular neoprene with a neoprene skin surface and nylon lining. Since the radius of operations of carrier-based aircraft often places Navy pilots in radically opposite environmental conditions, ventilation must be provided for any impermeable suit assembly which they wear. The problem has been solved by using controlled orifice ventilation channeling, coupled with the strategic location of carefully selected spacer materials. To meet the urgent need of A–1 pilots for increased life preserver buoyancy to support the weight of increased personnel survival equipment, ACED has also developed a new inflatable life preserver designated the MK–6. It has 65 pounds of buoyancy and is designed as an across-the-board replacement for other previously used life preserver vests which have fewer pounds of buoyancy. These and related accomplishments have greatly enhanced the Medical Department's support of military operations.

The issuance of this publication approved by the Secretary of the Navy on 4 May 1964.

MANAGEMENT OF BLEEDING OESOPHAGEAL VARICES

Roger Williams, MD MRCP, and John Dawson,† MS FRCS, Brit Med J 1(5583):35–37, January 6, 1968.*

Patients with bleeding oesophageal varices die from exsanguination or liver failure or a combination of these factors. The development of liver failure is inevitable if bleeding is allowed to continue, and the first aim of treatment must be to stop haemorrhage by the fastest and simplest method available. Unfortunately bleeding tends to recur unless the portal venous pressure can be permanently lowered; but in practice the timing and choice of correct operation are difficult. Throughout the care of these patients medical and surgical therapy are closely linked, and the importance of combined consultation of physician and surgeon with formulation of a definite plan for each patient cannot be overstressed.

Initial Assessment

The differential diagnosis of the various types of portal hypertension and cirrhosis is beyond the scope of this article. In patients who are bleeding from varices it is important to determine as soon as possible whether the cause is: (1) extrahepatic portal hypertension, due to thrombosis of the splenic or portal vein; or (2) intrahepatic portal hypertension due to cirrhosis—by far the commoner cause in Britain.

The chances of successfully controlling the acute bleed and the prospect of long-term survival are higher in the first group, though the types of surgery possible are more limited since a portacaval anastomosis with a few exceptions cannot be performed.

It is also important to be certain that the bleeding is coming from varices. Cirrhotic patients have an increased incidence of peptic ulcer, and in various series published from America more than half the cirrhotic patients admitted with bleeding have either an alcoholic gastritis or a chronic peptic ulcer. In Britain alcoholism is a less common cause of cirrhosis, so probably more patients with cirrhosis who bleed do so from varices. Though a barium examination is often helpful direct visualization of a bleeding point at oesophagoscopy is the only certain way of making the diagnosis. The procedure is unpleasant for the patient and bleeding may have stopped by the time of examination, so that our practice is to perform oesophagoscopy or gastroscopy only when there is clinical doubt as to the site of bleeding. The control of bleeding by a Sengstaken tube is a useful confirmatory test.

Biochemical tests such as the bromsulphalein (B.S.P.) retention have also been suggested as aids to differential diagnosis. However, Enquist *et al.* showed in a large series that B.S.P. excretion can be impaired in patients with acute gastrointestinal haemorrhage not due to liver disease—presumably as a result of a decreased liver blood flow. The finding of a raised blood ammonia level points to underlying liver disease or an extensive collateral circulation or both, but again does not prove that it is the varices which are bleeding.

Treatment of Acute Bleeding

Hemorrhage causes decreased hepatic blood flow, and the resulting liver cell anoxia together with the absorbed load of nitrogenous breakdown products from the blood draining the bowel frequently produces hepatic encephalopathy.

The principles of treatment are to restore the blood volume, to prevent breakdown of blood within the bowel, and to arrest the haemorrhage.

Restoration of Blood Volume

Adequate blood transfusion is essential to prevent further impairment of liver cell function. If possible fresh blood should be used for this will make up, albeit temporarily, the deficiency of platelets and clotting factors usually present in cir-

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rhosis. Vitamin K^1 (10 mg. intramuscularly daily) should also be given routinely.

Prevention of Protein Breakdown

The bowel lumen should be emptied by purging with magnesium sulphate orally and by enemata until normal bowel contents are obtained. Neomycin (1 g. four-hourly) should be given by mouth to decrease the bacterial breakdown of blood in the gut. Sedation is best avoided, but if the patient is greatly distressed phenobarbitone (60–200 mg. intramuscularly), which is largely excreted by the kidney, or chlorpromazine (50–100 mg. intramuscularly) is probably the least harmful. Occasional patients—usually those with extrahepatic obstruction—will stop bleeding spontaneously or after blood transfusion.

Arrest of Haemorrhage

Vasopressin lowers portal blood flow and pressure as a result of vasoconstriction of the splanchnic arterioles. Vasopressin is given as an intravenous infusion of 20 units in 100 ml. of 5 percent dextrose over 20 minutes. The effect lasts up to an hour. Initially there is also systemic arteriolar constriction with transient pallor of the skin and a rise in arterial blood pressure. Intestinal colic is another immediate effect, which may be useful in emptying the bowel of blood. The dose can be repeated after four hours, but its efficacy tends to decrease with successive doses. The use of vasopressin is contraindicated in patients with cardiac ischaemia, and another disadvantage is that the reduced hepatic blood flow may further impair the circulation to the cirrhotic nodules. The synthetic derivative phenylalanine-lysine-vasopressin (Octapressin) has less effect on the systemic circulation, but its advantages over vasopressin have not been established in a controlled trial.

Balloon Tamponade.—The Sengstaken tube with its gastric and oesophageal balloons was introduced in 1950, and much has been written about its use. Traction is advised by some to keep the gastric balloon in position in the fundus of the stomach, and this can be judged by screening the patient during inflation of the balloons. The tube is undoubtedly effective but is unpleasant for the patient, and there is also a risk of pulmonary complications and oesophageal ulceration. Repeated pharyngeal suction to remove saliva and other secretions is required, and on no account should the balloons be left inflated for more than 24 to 36 hours. Some workers find that a single gastric balloon is sufficient, and suggest that the pressure of the balloon against the diaphragmatic crura stops the blood flow from the gastric veins into the oesophageal varices.

Gastric Hypothermia.—Hypothermia is produced by the circulation of an ethanol-water mixture through a gastric balloon at a temperature of 0°C. Cooling is maintained for periods of 24 to 72 hours. There is no change in portal pressure, and bleeding probably stops as a result of local vasoconstriction of small vessels. Cooling is tolerated better than the Sengstaken tube but shares the high incidence of pulmonary complications.

Published results show that any of these three techniques will stop bleeding in 70–80 percent of patients. Unfortunately their effect tends to be temporary, and bleeding recurs particularly in those patients with severe hepatocellular failure. Pitressin therapy is the simplest and least distressing to the patient, and as illustrated in the figure our practice is to use it once in all patients unless there are specific contraindications. If bleeding stops and does not recur within the subsequent weeks the patient can be assessed for definitive surgery.

If bleeding recurs it should be controlled with the Sengstaken tube (or gastric hypothermia if available) and the patient prepared for surgical intervention. When to operate in the individual patient is a difficult decision. There is no doubt that with each further bleed and subsequent resuscitation the general condition and liver function of the patient deteriorates and the chances of a successful outcome get less. Operation should therefore be done early rather than late, and every patient should be considered—except for those with deep jaundice, ascites, or coma, in whom bleeding is but one manifestation of terminal liver failure.

Operations to Stop Bleeding

Surgical ligation of varices is probably the simplest and most effective method available. The left chest is opened through the bed of the eighth rib and the inferior pulmonary ligament dissected upwards to expose the pleura overlying the lower oesophagus. The large collateral veins around the lower oesophagus are best suture-ligated to prevent troublesome bleeding during mobilization of the oesophagus. If the patient has ascites care should be taken not to open the diaphragm or to disturb the oesophageal hiatus, as this may allow ascitic fluid to accumulate in the pleural space and cause much difficulty in the postoperative period.

Once the oesophagus is mobilized a soft clamp is placed across the oesophago-gastric junction to lower the pressure within the varices. These may then be dealt with in either of two ways: (1) *The Boerema-Crile Operation.*—The lower oesophageal lumen is entered via a longitudinal incision. The columns of varices are then under-run with a continuous atraumatic catgut suture. The oesophagus is then closed in layers with catgut and a chest drain inserted. (2) *The Milnes Walker Operation.*—The muscle of the lower oesophagus is divided longitudinally down to the mucosa. The mucosal tube together with the varices which lie in the submucosa is then dissected free. This tube is then divided transversely as low down as possible and resutured with a continuous catgut suture. This suture and the subsequent healing process in the mucosal layer occlude the varices. The two suture lines lie at right angles to one another so that the closure is potentially safer than in the Boerema-Crile operation. The oesophageal clamp should be released before the oesophagus is closed, to confirm that the bleeding has been stopped whichever operation is done.

After both these operations a gastrostomy is useful for feeding. No oral fluid is given for about five days, at which time a gastrografin swallow will confirm that the oesophagotomy closure is sound. The avoidance of a nasogastric tube allows the patient to co-operate with the postoperative chest physiotherapy more readily. It is usual for the patient to have a low-grade fever for some days, which may be due to thrombosis of the varices.

Other Methods.—An emergency portacaval shunt is occasionally worth considering in the patient with excellent liver function in whom the portal vein is known to be patent. Even in such cases the mortality rate will be higher than that for an elective shunt, and a more prudent course is to control bleeding by a simple ligation and do the shunt at a later date.

Another technique which has been employed is cannulation of the thoracic duct. The duct is exposed under local anaesthesia through an incision above the medial end of the left clavicle. Drainage of the lymph reduces the portal pressure. Variceal haemorrhage stopped in 8 out of 13 patients treated in this way by Dumont and Witte. However, the cannula tends to get blocked and bleeding usually recurs.

Prevention of Further Bleeding

Though a few patients do not re-bleed for a number of years after a ligation of varices the majority do, and all should be assessed and considered for definitive surgery. The operation which confers the best long-term protection against further haemorrhage is the portacaval shunt. Ideally the patient should be: (1) less than 50 years old; (2) not jaundiced; (3) have a serum albumin of greater than 3 g./100 ml.; (4) show no neuropsychiatric disturbance even during the haemorrhage. Relatively few patients fulfill these criteria, and many surgeons accept less favorable patients knowing that the mortality and morbidity of the operation will be increased. It is important to remember that signs of liver failure developing during or after a bleed may improve once haemorrhage has been controlled. Even the portal pressure can fall with medical treatment, particularly when cirrhosis is accompanied by marked fatty change as in the alcoholic.

Portal Venography.—The techniques of percutaneous trans-splenic venography is relatively simple and the portal pressure can be measured at the same time, but it cannot be performed if the prothrombin time is more than two seconds prolonged over normal. Occasionally all the contrast medium is diverted into collateral channels and the portal vein does not fill even though patent. This happened in 6.5 percent of a series of 904 splenic venograms reported by Burchell *et al.*, though in the majority of these anatomical patency was subsequently proved at operation. In such cases or in patients in whom splenic venography is contraindicated the technique of arterio-portography is of value. The coeliac axis or superior mesenteric artery is selectively catheterized and serial films taken of the arterial and venous phases after injection of contrast medium. Superior mesenteric arterio-portography is particularly useful in patients who have had a splenectomy. Some surgeons prefer to do venography and pressure measurement at the time of operation. However, this prolongs operating time, the pressure is lower than that recorded preoperatively, and it is preferable to have the information beforehand.

Shunt and Transection Operations

A portacaval shunt is usually done by anastomosing the end of the portal vein to the side of the inferior vena cava. A side-to-side anastomosis may be technically more difficult and may be associated with a higher incidence of post-shunt encephalopathy. It should be noted that all other shunts—for example, splenorenal and mesenteric-caval—

are in effect side-to-side anastomoses, so that the whole of the portal blood is not diverted from the liver.

In patients with extrahepatic portal hypertension, either a splenorenal or a mesenteric-caval shunt may be the only type of decompression possible. The thrombosis rate after splenorenal shunt, even if the vein is more than 1 cm. in diameter, is higher than after a portacaval shunt. A splenorenal shunt may also be done in cirrhotic patients who have secondary thrombosis of the portal vein or in the few patients in whom secondary hypersplenism is the major problem.

In cirrhotic patients who are unfit for shunt surgery, or in children with extrahepatic block (in whom the splenic vein is too small for a splenorenal shunt) some degree of protection against further haemorrhage may be conferred by a transection operation—either the Milnes Walker type already described, or the more extensive portaazygos disconnexion described by Tanner. In this procedure all the external vascular connexions of the lower 5 cm. of the oesophagus and the upper 5 cm. of the stomach are divided. The upper stomach is then transected and re-anastomosed. This is often a difficult and prolonged operation, and a thoraco-abdominal approach may be necessary. Resection of the lower oesophagus to remove varices with oesophagogastric anastomosis has been used with success, especially in patients with an extrahepatic block. Like transection procedures these do not affect the underlying portal hypertension. The injection of sclerosant solution into the varices or into the submucosa around the varices has also been employed, but there are no controlled trials of its use.

Results

There is no doubt that a successful shunt can prevent further bleeding. Grace and his colleagues, who have recently analyzed 154 papers in the world literature, found that the incidence of recurrent bleeding in 1,020 patients following a shunt operation was 6.7 percent (portacaval anastomosis 2.8 percent, splenorenal 19 percent). The overall incidence of hepatic encephalopathy was 19.0 percent and the incidence was higher after a portacaval anastomosis than after a splenorenal shunt. Clinical manifestations of hepatic encephalopathy varied from mild impairment of intellect to disabling organic neurological syndromes. The development of encephalopathy must to some extent reflect the progressive nature of the underlying liver disease, but there seems little doubt that the incidence is higher after shunt operations. Indeed, this is the price that some patients pay for the prevention of further haemorrhage. The symptoms in many of these patients, however, are relatively easily controlled by dietary protein restriction and neomycin therapy.

The reported figures for long-term survival vary, but in three large series from America between 50 and 65 percent of patients were alive five years after a portacaval anastomosis. In a recent analysis of 242 cases Hunt found a five-year survival of 48 percent and a ten-year survival of 27 percent.

Although the prognosis in selected groups of good risk patients treated by shunt operations is good, the overall results reported for bleeding varices are less encouraging. Hislop and colleagues found that 34 of 63 patients admitted with their first bleed from varices died, and in Sherlock's series 40 of 120 cirrhotic patients died within a year of their first haemorrhage. Indeed, according to Grace *et al.* there is little evidence at present to show that shunted patients survive longer than good risk cirrhotic patients who have bled but not had a shunt performed. These authors also note that the most enthusiastic claims for shunt surgery were made by those workers with poorly controlled series.

Very often patients have been considered for transection operations only when they have been deemed unsuitable for shunt surgery, and there are no controlled studies available. No further bleeding occurred in 14 of 25 cirrhotic patients with a portaazygos disconnexion reported by Tanner, and in 13 of 25 patients with extrahepatic portal vein obstruction treated by oesophageal transection by Milnes Walker. The greater risk of rebleeding may be compensated for by a lower incidence of serious encephalopathy, but whether this is so and whether survival is prolonged has not yet been answered.

Finally, no account of this subject would be complete without mention of the prophylactic portacaval shunt, the operation being done before bleeding has occurred. However, the results to date of two carefully controlled trials in America show that the overall survival of such patients does not differ significantly from that of controls, though the incidence of variceal bleeding is considerably decreased. Only one of the 68 patients with a prophylactic shunt has bled since the time of randomization as compared with 19 of the 73 in the control group. This is gained at the expense of an increased incidence of encephalopathy, the figures

being 25 percent for the shunted group and 5.5 percent for the controls. Here again one has to balance the disability to the patient of encephalopathy as opposed to recurrent bleeding, and this perhaps is one of the most difficult problems to evaluate at present.

(The omitted figure and references may be seen in the original article.)

"... AND GO LIGHT ON THE SODA."

B. Roe, MD, and B. Eiseman, MD.

Both in civilian and military practice, intravenous sodium bicarbonate usually is being administered on an empiric basis for the resuscitation of the severely injured. Objective evidence shows that this agent often is given unnecessarily or in excessive amounts, despite apparent rationale for its use.

Resuscitation of the injured inevitably involves the simultaneous use of many drugs and many procedures, making it difficult objectively to evaluate the effectiveness of a single uncontrolled measure. Thus, it is necessary to rely on laboratory evidence to support the contention that "sodium bicarbonate is better for shock than it is for ulcers." Critical evaluation is particularly important when such a drug may be harmful.

Major blood loss results in deficient tissue perfusion with consequent anerobic metabolism and metabolic acidosis. Associated interference with ventilation by thoracic injury or drugs that depress respiration might superimpose respiratory acidosis. Experience in the field, however,[1,2] demonstrates that even the seriously injured young combat casualty actually is in respiratory *alkalosis* from hyperventilation (caused by anxiety) when he is first treated for shock in a forward area. Blood gas analysis and blood pH determinations on these patients demonstrates that significant metabolic acidosis occurs only in the hopelessly moribund or after a relatively long period of untended hypotension. Prompt resuscitation with blood replacement usually reverses the development of acidosis before it reaches dangerous proportions.

Primary efforts to correct acidosis should be by re-establishing blood volume, good tissue perfusion, and good ventilation, rather than by a spasmodic response to use alkalinizing agents.

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Effects of Metabolic Acidosis

A little acidosis is not so bad. It doesn't hurt the heart. Cardiac output is not depressed by pure metabolic acidosis until pH is depressed below 6.7. Dowling[3] showed that a pH of 6.8 produced by adding hydrochloric or lactic acid in the cat did *not* reduce left ventricular contractility, heart rate, or blood pressure. There was, however, a decrease in systemic vascular resistance and a rise in pulmonary vascular resistance. Kittle[4] found that metabolic acidosis of pH 7.07 depressed cardiac output by only 20 percent. However, it is significant that the consequences of mild metabolic acidosis alone are greatly compounded when oxygenation is impaired; both Clowes[5] and Dowling[6] showed that the *combination* of hypoxia and acidosis severely impairs myocardial contractility.

Respiratory Acidosis

Inadequate ventilation with subsequent carbon dioxide accumulation (elevated pCO_2) increases cerebral, coronary, and renal artery blood flow[4] regardless of blood pH. Anderson[7] showed that respiratory acidosis even as low as pH 6.9 increased cardiac output. Such responses to acidosis are obviously protective—not detrimental—to a severely injured patient.

Catecholamine Response

The normal vasomotor responses of adrenalin and other catecholamines are thought by some to be impaired in the presence of acidosis. Weil[8] found that respiratory acidosis decreased the pressor response. Dowling,[3] on the contrary, found that neither respiratory nor metabolic acidosis as low as pH 6.80 altered the inotropic response of levoterenol or epinephrine.

Effect of Acidosis on Delivery of Oxygen to the Tissues

According to the Bohr formula, acidosis promotes oxyhemoglobin dissociation as oxygen is more easily

released from hemoglobin. This effect of acidosis partially compensates for decreased cellular perfusion so that a smaller volume of blood flow can satisfactorily oxygenate the tissues.

Moderate acidosis in more ways than one thus is a compensatory homeostatic mechanism and its reversal with sodium bicarbonate is not a totally unmixed blessing.

Effects of Sodium Bicarbonate Administration

The standard 50 cc ampule of sodium bicarbonate contains 44 meq of sodium. In rather wild desperation, 15 ampules (or even double this number) have been given to a casualty within 12 hours after serious injury. Fifteen ampules equals 660 meq or almost 50 percent of the total body extracellular sodium. In a shocked patient oliguria may make it difficult to lighten this load. It is obvious that such blind administration of large volumes of hypertonic sodium solution can quickly produce a significant sodium and fluid overload. Simultaneous injudicious use of large volumes of sodium lactate solution in initial resuscitation may compound the difficulty and precipitate pulmonary edema even in the healthy, young casualty. With such a volume of sodium and water aboard and with an unsatisfactory urinary output, it may be exceedingly difficult to bail out the excess salt water from the patient's lungs. Edema around the eyes, ankles, and sacrum are of no consequence, but when the fluid seeps into the alveoli a potentially lethal vicious cycle is underway.

Many factors probably contribute to pulmonary edema that occasionally follows nonthoracic trauma. At the moment we are not sufficiently wise to be able to avoid all of these factors. We must, therefore, carefully avoid any known factor, such as sodium overload, which might precipitate this syndrome.

Trained combat surgeons are painfully aware of the necessity for prompt restoration of normal intravascular volume and good ventilation. They know that this is the best way to overcome acidosis. They are, however, occasionally seduced by a simple short cut for re-establishing a "normal" pH by simple addition of an alkali. As with most simple solutions, this attractive short cut has inherent complications.

Proper use of sodium bicarbonate in a research unit or in a well equipped hospital is simple: Sodium bicarbonate is given along with other means for resuscitation and ventilation when the blood pH becomes excessively low and the pCO_2 becomes elevated. Most surgeons responsible for initial resuscitation of the combat casualty have no such luxury of equipment. They must use clinical judgment. They now should be forewarned with the following facts.

1. Even the seriously injured combat casualty, unless obviously moribund, is usually not in profound acidosis soon after his injury.

2. The physiologic effects of *mild* acidosis have some beneficial effects in combating shock.

3. Sodium bicarbonate overload has inherent dangers and can significantly contribute to the onset of pulmonary edema.

This knowledge should stay or, at least, temper the hand of those who have in the past occasionally used sodium bicarbonate indiscriminately.

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MISTAKEN PSYCHIATRIC REFERRAL OF OCCULT SERIOUS CARDIOVASCULAR DISEASE

M. Irené Ferrer, MD, New York, Arch Gen Psychiat 18(1):112–113, Jan 1968.

In recent years it has become apparent that a number of patients with serious cardiovascular disease are being mistakenly referred by their internists to psychiatrists. In turn the latter search vainly for the correct psychiatric diagnoses when, in fact, they should reallocate the patient in order to secure for him specialized and intensive medical investigation. A simple medical evaluation in these situations is unlikely to uncover the correct state of affairs. Hence, the patient will be as far from help as before he or she consulted not one, but at least two, physicians considered to be relatively expert.

There are certain symptoms in cardiovascular disease which may exist without objective confirmation or ready explanation and hence are often assigned to a functional nonpathologic origin. In particular there are two groups of patients, those with intermittent complete atrioventricular (AV) block and those with multiple pulmonary emboli, who, after an initial medical visit or two, are frequently referred for psychiatric help. In reality, however, they are suffering from serious medical diseases which, if undiagnosed, may be eventually fatal. This communication, therefore, is prepared in the hope of bringing these states once again to the attention of psychiatrists who may be able to redirect the patient toward a correct appraisal.

Intermittent complete AV block may precede the appearance of permanent block by several years. The subtlety of the early symptomatology of intermittent complete heart block is based upon the fact that the episodes of decreased cerebral blood flow, which are the basis for dizziness, faintness, fugue-like periods, short memory losses, brief syncopal moments, and the development of irritability and adverse personality changes, are short-lived at the outset. Thus, they are difficult to document unless the patient is being constantly monitored for changes in ventricular heart rate. There are four mechanisms responsible for slowing of cerebral flow in complete heart block: (1) One mechanism is the momentary complete AV block *without* the appearance of any ventricular impulse and hence complete ventricular arrest. Restoration of sinus rhythm with ventricular response soon occurs, however, or the patient obviously succumbs. (2) Momentary AV block *with* a ventricular focus coming to the rescue but firing at one half or one third the previous heart rate is another mechanism. During a period of accommodation to this bradycardia, the brain may be underperfused. (3) The appearance of paroxysmal ventricular tachycardia or fibrillation may occasionally occur in patients with intermittent as well as permanent complete AV block. During such bouts cerebral flow drops sharply. (4) When a patient with intermittent AV block, be this incomplete (with a 3:1 or 4:1 AV response) or complete, develops ventricular rates less than 25 to 30 beats per minute, symptoms will soon follow, as the rates per se are too slow for adequate organ perfusion.

The symptoms associated with intermittent heart block may be difficult for the patient himself to verbalize, hence creating considerable anxiety. Indeed some unfortunate subjects have been accused of being secret drinkers or drug addicts by their family or friends. This anxiety, of course, increases when he is told that "nothing is wrong medically." Intermittent heart block may exist for a number of years without any other signs of heart disease, eg, with a normal electrocardiogram when not in block, no abnormality of blood pressure, no murmur or gallop, and no cardiomegaly. It has also been our experience that a number of patients with intermittent complete AV block and Stokes-Adams seizures are admitted to neurological institutes with diagnoses of central nervous system diseases such as epilepsy, cerebral accident, or tumor.

A correct diagnosis of intermittent AV block is best made by monitoring the patient over a considerable period of time. Portable monitor units using recording tape are now available. These can be worn by a patient continuously for a number of days.

The second condition, multiple pulmonary emboli, is even more likely to be called a psychoneurosis, since documentation is more difficult by ordinary clinical means when the disease is first beginning. Predominantly but not exclusively a disease of young women, the embolic episodes first

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may occur at long intervals of weeks or even months. A brief and vague chest discomfort, perhaps associated with tachypnea which may not be perceived, is often all that marks the initial phase. Hemoptysis may never occur and cough is usually a late comer. Pleuritic pain is not necessarily noted and the chest x-ray remains within normal limits, as pulmonary infarcts, if produced at all, are too small to appear. It is not until late in the disease, often two to five years after its onset, that the pulmonary hypertension consequent to multiple vascular closures increases to the level sufficient to alter the size of the pulmonary arteries and right ventricle.

In taking the history of this illness it may be impossible to learn of the underlying gynecologic condition which provokes pelvic venous disease, one of the common etiologies for emboli, as the patient may not disclose a previous abortion or symptoms of pelvic inflammatory disease. Furthermore, pelvic examination is not always revealing. Venous disease of the legs, of course, is self evident and is the other frequent source for emboli. An undiagnosed gastrointestinal tumor with metastases, such as carcinoma of the body of the pancreas or stomach, can be another cryptic origin. As the embolic episodes grow more frequent, dyspnea usually begins periodically. By this time hyperventilation accompanies the episodes. Later it becomes chronic, thus remaining in evidence between attacks. With chronic hyperventilation there is usually chronic dyspnea.

Psychiatric help is usually sought for dyspnea and hyperventilation as well as the anxiety that can be extreme during the embolic attacks. Physical examination, x-rays of the chest, and early electrocardiogram may all be unrevealing. If one is to halt the embolic ravages of the pulmonary circulation before the vascular changes become irreversible or before one of the occlusions is fatal, the disease must be diagnosed early.

To arrive at an early diagnosis, the first and completely essential step is to think of the possibility of its existence in patients with peculiar chest symptoms who appear to have no objective evidence of medical disease. This can be followed by special studies such as cardiac catheterization with angiocardiography and lung scans. If the disease has existed for some time, one may obtain transitory electrocardiographic evidence of right ventricular dilatation which is associated with the embolic shower, but this evidence is often fleeting and must be obtained by exquisite timing.

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BLOOD GAS AND ELECTROLYTE CHANGES IN HUMAN NEAR-DROWNING VICTIMS

Jerome H. Modell, MD, Joseph H. Davis, MD, Samuel T. Giammona, MD, Frank Moya, MD, and Joel B. Mann, MD, JAMA 203(5):337–343, January 29, 1968.

Twelve human near-drowning victims were treated, and their clinical courses were studied with particular attention given to electrolyte and blood gas changes. Ten of these patients made complete uneventful recoveries. The primary pathophysiological disturbance which necessitated emergency therapy was acute asphyxia with persistent arterial hypoxemia and acidosis. Initially the hypoxia appeared to be due to perfusion of nonventilated alveoli. Persistent arterial hypoxemia was present, however, even after a significant intrapulmonary shunt could no longer be demonstrated. The plan of management for each patient should be determined by individual laboratory and clinical studies.

During the past few decades, considerable emphasis has been placed on the serum electrolyte changes that occur during drowning. In a retrospective study published in 1963, however, Fuller was unable to document significant electrolyte changes in human near-drowning victims. Recent experiments with animals have shown that the electrolyte changes following aspiration of both fresh water and sea water are related directly to the

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quantity of water aspirated. In untreated animals which survived these experiments, electrolyte values spontaneously returned to normal. The common denominator in all animals, regardless of the composition or volume of fluid aspirated, was the onset of acute asphyxia with persistent arterial hypoxemia and acidosis. The following clinical study was undertaken to correlate laboratory findings of studies of animals with changes observed in human near-drowning victims.

Methods.—Twelve human near-drowning victims, six who had aspirated chlorinated fresh water, and six who had aspirated sea water, have been treated during the past three years at the University of Miami-Jackson Memorial Hospital. The sea-water victims were retrieved from the Atlantic Ocean beaches of southeastern Florida, and the fresh water victims were rescued from chlorinated fresh water pools. For all patients who had nearly drowned in fresh water, a sample of pool water was obtained and analyzed for electrolyte concentrations. Medical therapy was supervised by the authors for 11 patients from the moment they first entered the hospital. Consultation was not obtained until 18 hours after admission for the 12th victim (case 4). Initial emphasis was on immediate therapy, and the data were obtained without compromising the clinical course of the patients.

Aliquots of venous blood were drawn within minutes of each patient's arrival to the emergency room and were placed in tubes containing sodium citrate for whole blood studies, or in dry tubes for serum studies. Whole blood was analyzed for hemoglobin concentration by the cyanmethemoglobin method, and for hematocrit value with a Guest-Weichselbaum microcapillary centrifuge. The blood was then centrifuged, and the plasma was removed and analyzed for hemoglobin content by a modification of the Bing and Baker technique. Serum concentrations of sodium and potassium were determined on a flame photometer; a commercial serum preparation was used as a control. The serum chloride level was determined on the Buchler-Cotlove chloridimeter.

Seven patients (five fresh water and two sea water victims) had arterial blood drawn for analysis of pH, carbon dioxide tension (Pco_2), and oxygen tension (Pao_2) within 10 to 20 minutes after arrival at the emergency room. Two additional patients (both sea water victims) had blood drawn for determination of pH, Pco_2 and Pao_2 after initial therapy was given. The remaining three patients (two sea water victims, one fresh water) were treated before this phase of the study was initiated. Arterial blood was drawn anaerobically in glass syringes which contained heparin sodium and was analyzed within five to ten minutes with direct reading electrodes at 98.6 F (37 C).

Results

General Clinical Course of Victims Rescued From Chlorinated Fresh Water.—The ages of the six victims who nearly drowned in chlorinated fresh water ranged from 3 to 14 years. They were all apneic when rescued and required mouth-to-mouth resuscitation. One patient (case 6) required closed-chest cardiac massage. When admitted to the emergency room all six were unconscious, tachypneic, and obviously cyanotic. The initial therapy consisted of ventilatory support, ranging from simple oxygen administration to controlled ventilation with automatic ventilators, correction of acid-base imbalance, and treatment of aspiration pneumonitis. Fluid and electrolyte therapy was guided by concurrent laboratory data, intake and output balance, and central venous pressure value. Five of the six patients made complete uneventful recoveries; the sixth (case 6), although regaining consciousness for approximately 48 hours while ventilation was being controlled, died 85 hours after admission to the hospital.

Table 1.—Blood Values of Chlorinated-Fresh-Water Near-Drowning Victims on Admission to Hospital and Electrolyte Concentration of Water From Which Each Patient was Recovered

	Venous Blood Sample						Water Sample		
Case No.	Hgb (gm/ 100 ml)	Hct (vol%)	Na^+ (mEq/ liter)	Cl^+ (mEq/ liter)	K^+ (mEq/ liter)	Plasma Hgb (mg/ 100 ml)	Na^+ (mEq/ liter)	Cl^- (mEq/ liter)	K^+ (mEq/ liter)
5	14	44	139	94	3	208	2	4	0
6	14	42	142	99	3.3	500	3	0	0.2
7	12	38	136	101	4.5	25	34	20	0.8
8	13	39	137	100	3.4	8	4	6	0.2
9	13	39	131	94	4.1	17	4	5	0.1
12	12	36	139	101	5.8	81	10	6	0.2

Table 2.—Laboratory Values of Blood Drawn From Victims Who Nearly Drowned in Sea Water* Minutes After Admission to Hospital

Case No.	Hgb (gm/100ml)	Hct (vol%)	Na^+ (mEq/liter)	Cl^- (mEq/liter)	K^+ (mEq/liter)	Plasma Hgb (mg/100 ml)
1	18	51	160	115	3.8	2
2	12	38	142	100	4.3	0
3	14	41	153	116	4	4
4	12	37	149	120	3.5	0
10	13	39	156	118	4.8	0
11	12	36	154	112	3.8	0

* Average sea water electrolyte concentration in mEq/liter: sodium, 597; chloride, 559; and potassium, 10.7.

General Clinical Course of Sea Water Victims.—Three sea water victims were adults and three were children. All but one (case 4) required mouth-to-mouth ventilation on the beach. Two patients (cases 1 and 3) were still semicomatose on admission to the emergency room, and all had varying degrees of respiratory distress. The five patients who were treated primarily for hypoxia and aspiration pneumonitis eventually made uneventful recoveries. The sixth patient (case 4), who was awake and talking on admission to the hospital, received meticulous fluid and electrolyte correction therapy; however, pulmonary therapy consisted primarily of an oxygen tent. Approximately 18 hours after admission to the hospital, the patient was unconscious and gasping for breath. Arterial blood was drawn and showed a pH of 7.10 and a Pao_2 of 34 mm Hg. The child died ten minutes after this blood sample was drawn, and could not be resuscitated in spite of artificial pulmonary and circulatory support.

Hemoglobin, Hematocrit, and Electrolyte Changes.—Hemoglobin values, hematocrit readings, and electrolyte concentrations of the blood drawn from the fresh water victims are listed in Table 1. The hemoglobin values and hematocrit readings were normal in all patients, despite free plasma hemoglobin values ranging from 8 to 500 mg/100 ml, indicating significant hemolysis in some. Three patients (cases 6, 9, and 12) showed a fall in hemoglobin concentration to 10.6 to 11 gm/100 ml, and in the hematocrit reading to 32 percent to 33 percent within 24 hours. The serum concentrations of sodium and chloride were found to be normal in all but one patient (case 9, sodium, 131 mEq/liter). The potassium concentration was normal in two, high in one, and low in three patients. An electrocardiogram taken at this time on patient 12 (potassium level was 5.8 mEq/liter) showed an increase in the amplitude of the T wave, which responded immediately to simultaneous correction of acidosis and hypoxia, and the administration of 200 mg of gluconate calcium. The concentrations of sodium, chloride, and potassium of the pool water from which the patients were rescued are listed in Table 1 with the corresponding blood values.

The hemoglobin values, hematocrit readings, and serum electrolyte concentrations of blood drawn from the sea water victims are listed in Table 2. All but one patient (case 1) had normal hemoglobin and hematocrit values which remained essentially unchanged throughout hospitalization. The concentrations of serum sodium and serum chloride were moderately elevated in most patients. The serum potassium level was normal in three patients and low in three patients. Concentration of plasma hemoglobin was negligible. Although the concentration of electrolytes in sea water vary slightly with the tide, average values from the area where these patients were rescued are specified in Table 2.

Blood Gas Values.—The values for pH, Pco_2, and Pao_2 of the seven victims who had arterial blood drawn in the emergency room are listed in Table 3. Six of these seven patients were severely acidotic at the time of admission; the lowest pH recorded was 6.95. The Pco_2 ranged from 29 to 64 mm Hg. The base excess concentrations, determined by the Siggaard-Andersen alignment nomogram show that four of the seven had a severe metabolic acidosis. Two patients (cases 6 and 7) each received 44.6 mEq of sodium bicarbonate ($NaHCO_3$) immediately prior to the drawing of these initial blood samples. The degree of acidosis and base deficit may have been even more severe in these patients prior to administration of sodium bicarbonate.

It was considered to be clinically safe to withdraw supplemental oxygen inhalation therapy long

Table 3.—Arterial Blood Values of Near-Drowning Victims Within 10 to 20 Minutes of Arrival to the Hospial Emergency Room

Case No.	Type of Water	pH	P_{CO_2} (mm Hg)	Base Excess (mEq/liter)	P_{O_2} (mm Hg)	Prior or Concurrent Therapy
6	Fresh	7.05	59	−16	40	100% O_2 IPPB* (patient weighed 50.8 kg [112 lb]) 44.6 mEq $NaHCO_3$
7	Fresh	7.21	37	−12.5	175	100% O_2 IPPB (patient weighed 20 kg [44 lb]) 44.6 mEq $NaHCO_3$
8	Fresh	7.28	54	−3	35	Loosely fitting O_2 mask
9	Fresh	7.19	29	−16	108	IPPB with 40% + O_2
10	Sea	7.35	47	−1	45	Room air
11	Sea	7.29	49	−4	364	100% O_2 IPPB
12	Fresh	6.95	64	−19	245	100% O_2 by mask

* Intermittent positive pressure breathing.

enough to get an arterial blood sample from only one patient (case 10) who was breathing room air. The severity of her hypoxia is apparent from the P_{aO_2} of 45 mm Hg observed. A second patient (case 8) had a P_{aO_2} of 35 mm Hg while a loosely fitting BLB oxygen mask was in place. A third patient (case 9) had a P_{aO_2} of 108 mm Hg recorded while his ventilation was being controlled with a pressure limited respirator via a cuffed, endotracheal tube. The respirator was driven by compressed oxygen and was set on air-oxygen mix at the time. Although the inspired oxygen concentration was not measured directly, it can be assumed to be between 40 per cent and 100 percent with this apparatus, depending upon the compliance of the patient's lung and thorax. The remaining four patients received 100 percent oxygen for at least 15 minutes before the blood sample was drawn. With an alveolar oxygen tension (P_{aO_2}) ranging from 649 mm Hg to 667 mm Hg ($P_{aO_2} = P_B - P_{H_2O} - P_{CO_2}$), the P_{aO_2} values observed ranged from 40 mm Hg to 364 mm Hg. The calculated alveolar-arterial oxygen gradient ($A - aDO_2$) in these four patients was as follows: 300 mm Hg, case 11; 410 mm Hg, case 12; 501 mm Hg, case 7; and 640 mm Hg, case 6. These data, in the presence of 100 percent oxygen administration, suggest a severely abnormal ventilation-perfusion ratio ($Va/Q = 0$) due to the shunting of blood through perfused, but nonventilated, alveoli.

Although it is not the purpose of this communication to present individual case histories, a review of serial blood gas values in a few patients will help to explain the relationship between the basic pulmonary lesion involved and the necessary treatment. Table 4 illustrates the blood gas levels in some typical near-drowning victims. In the first two patients (cases 11 and 12), the alveolar-arterial oxygen gradient was measured periodically after 15 to 20 minutes of 100 percent oxygen administration via a nonrebreathing system. Assuming the arterial-venous oxygen content difference ($Ca_{O_2} - C\bar{v}_{O_2}$) to be 5 vol%, we calculated the proportion of cardiac output which was being shunted through perfused, but nonventilated, alveoli on the patient's admission to be approximately 15.7 percent in one patient and 20.3 percent in the other. This modified shunt equation was used:

$$\frac{Qs}{Q_T} = \frac{(A - aDO_2)\ (0.0031)}{(Ca_{O_2} - C\bar{v}_{O_2}) + (A - aDO_2)\ (0.0031)}$$

It took approximately 39 hours in one patient and 24 hours in the other before the shunt (while the patient was breathing 100 percent oxygen) decreased to a level of approximately 7 percent. A normal P_{aO_2} value (91 mm Hg) was observed while the first patient was breathing room air shortly thereafter (40 hours after aspiration). The second patient, however, was obviously still hypoxic while breathing room air (P_{aO_2} was 59 mm Hg). Oxygen therapy was continued, and the following day the patient showed only a slight improvement when tested while breathing room air (P_{aO_2} was 69 mm Hg). Seventy-two hours after aspiration, a more normal value was obtained (P_{aO_2} was 86 mm Hg), and supplemental oxygen inhalation was discontinued. This delayed return to a normal P_{aO_2} while the patients were breathing room air was not unusual in these individuals. Arterial hypoxemia was still present in one patient (case 10) on the fifth day following aspiration. The patient refused to have additional studies after that time.

Table 4.—Arterial Oxygen Tension After Near-Drowning

Case No.	Type of Water	Hours After Aspiration	P_{O_2} of Patients Breathing 100% O_2 (mm Hg)	A—aDO_2 of Patients Breathing 100% O_2 (mm Hg)	P_{O_2} of Patients Receiving Therapy or Breathing Room Air (mm Hg)
11	Sea	1	364	300	...
		2	...	...	210; 40% O_2, nonrebreathing mask
		14	390	285	...
		24	...	...	101; Face hood with 40% O_2 minus dilution
		39	525	143	...
		40	...	...	91; Room air
12	Fresh	0.5	245	410	...
		2	324	344	...
		5	...	...	122; 58% O_2 nonrebreathing mask
		24	514	153	...
		25	...	...	59; Room air
		48	...	...	69; Room air
		72	...	...	86; Room air
7	Fresh	1	175	501	...
		2	...	...	82; 60% O_2 nonrebreathing mask
		3	320	355	...
		20	...	...	79; Room air
		48	...	...	95; Room air
9	Fresh	1	...	...	108; IPPB-O_2 40% +
		24	...	...	67; Room air
		48	...	...	88; Room air
10	Sea	1	...	...	45; Room air
		48	...	...	52; Room air
		72	...	...	58; Room air
		96	...	...	69; Room air

While the chest roentgenograms of some patients showed the diffuse infiltrate described as the post-immersion syndrome, this was not always the case.

Report of Cases

Case histories of patients who died are as follows:

Case 4.—This case clearly illustrates the importance of immediate ventilatory care. This 6-year-old boy is the only one of the 12 patients who was never apneic nor unconscious after rescue. Electrolyte determinations were done immediately after his admission to the hospital, and the sodium and chloride concentrations were found to be elevated. Therapy with fluids administered intravenously was monitored by repeated electrolyte determinations. Within three hours, all electrolyte values were normal. Respiratory therapy was limited to an oxygen tent with an oxygen flow rate of approximately 6 liters per minute, and intermittent positive pressure breathing (IPPB) therapy every four hours. The therapist reported that although the child was lying still in his tent prior to IPPB treatment, he was extremely difficult to arouse. As the treatment progressed, his muscle tone increased, and he began to resist the therapy. The IPPB therapy was discontinued, since it seemed to excite the child. We were called in for consultation approximately 18 hours after the child was admitted to the hospital. At that time he was comatose, cyanotic, and gasping. Arterial blood was drawn and direct inhalation of 100 percent oxygen was started immediately. Within ten minutes, however, as the blood gas determinations were being done (pH, 7.10; P_{aO_2}, 34 mm Hg), the child died. Mechanical ventilation and circulation were attempted in combination with appropriate drug therapy for approximately one hour without success.

At autopsy the right lung weighed 470 gm and the left, 370 gm, (three to four times normal weight). The entire right lung and most of the left had an increased consistency and a reddish-brown purple color. Copious quantities of pinkish frothy fluid could be expressed from the lower airway and cut surface of the lung. Hematoxylin-eosin stained sections revealed a diffuse, intra-alveolar, pink, finely granular deposit characteristic of proteinaceous edema fluid. Thin, pink hyaline membranes were prominent within alveoli, and thicker membranes were seen in the alveolar ducts. Intra-

alveolar hemorrhage was prominent, but variable in intensity and distribution. Less prominent were occasional areas of peribronchiolar interstitial, and intra-alveolar neutrophilic infiltration. One section taken through an aerated portion of the left lung revealed markedly distended alveoli and respiratory ducts, with some focal interstitial emphysema. The pathological findings were summarized as an outpouring of proteinaceous edema fluid and erythrocytes, with condensation of protein into hyaline membranes, but with only slight neutrophilic response.

Case 6.—The second patient who died was a 14-year-old, 50.8-kg girl whose arm had been caught in the bottom drain of a swimming pool. The time she remained underwater was estimated to be ten minutes by poolside observers and rescuers. When removed from the pool, the patient was apneic and pulseless. Mouth-to-mouth ventilation and closed-chest cardiac massage were instituted immediately and continued in the ambulance on the way to the hospital. During the ambulance ride, spontaneous circulation and ventilation returned. On admission to the hospital she was cyanotic, cold, and clammy; and pink, frothy material poured out of her nose and mouth. Intubation was done, and the lungs were mechanically ventilated with inspired oxygen in a concentration of 100 percent. Sterile suction of the trachea was done repeatedly, and alcohol aerosol was delivered by intermittent nebulization to counteract the foam. The hemoglobin level, hematocrit reading, and electrolyte concentrations of blood drawn in the emergency room were all normal. The plasma hemoglobin concentration was 500 mg/100 ml. Arterial blood drawn after intravenous injection of 44.6 mEq of sodium bicarbonate and initiation of mechanical ventilation with 100 percent oxygen showed a pH of 7.05, Pco_2 of 59 mm Hg and Pao_2 of 40 mm Hg. The patient was transferred to the intensive care unit, where intra-arterial and central venous pressures were monitored, as were electrocardiographic and electroencephalographic activity. Assisted ventilation was maintained with a pressure-limited, volume-variable respirator for approximately two hours. She was then paralyzed with curare, and ventilation was controlled with a volume-limited, pressure-variable ventilator. She was also treated with steroids, antibiotics, sodium bicarbonate, digitalis, intravenously administered fluids, and mannitol. Renal function remained adequate, and within eight hours the urine and plasma were free of hemoglobin. During the first 24 hours, there was considerable fluctuation of both arterial and central venous pressure which were corrected by appropriate fluid therapy and blood administration. Approximately 24 hours after admission to the hospital the patient regained consciousness and, although she was unable to talk due to the presence of a nasotracheal tube, she was able to recognize her parents and communicate in sentences by moving her lips. Table 5 shows the Pao_2 values and the corresponding $A-aDO_2$ obtained at various times during the patient's therapy while her lungs were being ventilated with 100 percent oxygen. After the initial 24 hours, repeated attempts were made to decrease the inspired oxygen concentration. When it dropped below 90 percent, however, the Pao_2 would drop below 70 mm Hg and the patient would lose consciousness. The respiratory rate, tidal volume, and minute volume were adjusted frequently (up to a maximum rate of 20 respirations per minute, with a tidal volume of 1,000 ml) in an attempt to alter this response. The patient's blood gas profile continued to improve for approximately 30 hours, when, during a tacheal suction procedure, the child became extremely apprehensive and cyanotic. The entire episode lasted less than 30 seconds; however, she never again achieved the Pao_2 values obtained prior to that time. After 36 hours, arterial oxygen tension could not be maintained above 100 mm Hg except with obvious hyperventilation. This necessitated adding 2 percent carbon dioxide to the inspired gas to prevent hypocarbia and respiratory alkalosis. Her condition progressively deteriorated until she died 85 hours after admission.

At autopsy, there was 600 ml of dark proteinaceous fluid in the right pleural space and 550 ml in the left. Air under pressure, but without associated collapse of the stiffened lung, was observed in the right. The source of air could not be deter-

Table 5.—Pao_2* and $A—aDO_2$† in Drowning Victim (Case 6) While Ventilation Was Controlled With 100% Oxygen

Hours After Aspiration	Po_2 (mm Hg)	$A—aDO_2$ (mm Hg)
1	40	640
16	40	640
24	294	393
30	325	365
36	205	481
39	117	563
54	56	610
67	39	629

*Arterial oxygen tension.
†Alveolar-arterial oxygen gradient.

mined. The right lung weighed 690 gm and the left, 650 gm. Fibrinous exudate was present particularly upon the lower lobe of the right lung. An infarct with a diameter of 6 cm was present in the lower lobe of the right lung. Its center was undergoing liquification necrosis. The arterial branch to the infarcted area was completely occluded by a dark, adherent thromboembolus. The dependent portions of each lung were extremely dark purple in color, and had a nodular consistency. Cut sections showed a mottled lobular pattern almost completely devoid of air. Pressure produced thick, semimucoid, slightly purulent exudate from the surface.

Hematoxylin-eosin stained sections revealed no normal parenchyma nor any well-aerated sections. There were diffuse hyaline membranes lining the alveoli and alveolar ducts throughout all sections. Some alveoli also contained a very light pink proteinaceous exudate. Scattered intra-alveolar hemorrhage was present. Neutrophilic exudate was scant. The interlobular septae were edematous and focally infiltrated predominantly with lymphocytes and monocytes, a few neutrophils, and an occasional eosinophil. The bronchiolar epithelium was focally ulcerated, and the exposed submucosa was heavily infiltrated with neutrophils and monocytic cells. An occasional bronchiole contained a small fragment of aspirated vegetable matter. Focal areas of infarcted necrosis of alveolar septae were present. In these areas, bacterial clusters were prominent. The pleura was covered with a hemorrhagic and fibrinous exudate. In summary, the major histological findings were those of massive hyaline membrane formation, pulmonary thromboembolism with infarction, and irregularly distributed inflammatory exudate.

An attempt was made to extract pulmonary surfactant by the foam fractionation method, but none could be obtained. The lung was minced, and measurements were done on a surface tension balance as the surface area was compressed from 100 to 20 sq cm at a frequency of 1 cycle every 90 seconds. The lung extract had a minimum surface tension of 22 dynes/cm and maximum surface tension of 50 dynes/cm, compared with normal values of < 15 and > 45 dynes/cm respectively, indicating loss of normal surface activity.

Comment

It has been known since the turn of the century that movement of fluid and electrolytes across the alveolar capillary interphase occurs during drowning. The magnitude of this water transport and the severity of changes in serum electrolyte concentrations were stressed by Swann and associates, who studied these changes in dogs which were totally immersed in both fresh and sea water. In addition to acute asphyxia, animals immersed in fresh water showed a rapid onset of hypervolemia, hyponatremia, hypochloremia, hyperkalemia, and significant hemolysis; death was frequently caused by ventricular fibrillation occurring within moments of immersion. In animals which had been immersed in sea water, Swann et al observed a hypovolemia and an associated severe increase in the concentration of serum electrolytes. Although there is no question that marked shifts in fluid and electrolytes occur rapidly after total immersion, changes of this magnitude do not necessarily occur when smaller quantities of water are aspirated. The magnitude of change in electrolyte concentrations three minutes after experimental near-drowning in both fresh water and sea water has been shown to be proportional to the volume of fluid aspirated. In addition, in animals who survive near-drowning without therapy, electrolyte values return toward normal within one hour of aspiration. To produce severe electrolyte changes which persist and possibly contribute to the onset of ventricular fibrillation in dogs, at least 20 ml of fresh water per pound of body weight must be aspirated.

The review by Fuller suggests that human near-drowning victims do not show severe electrolyte changes after aspiration of either fresh or sea water. One objection to his study, however, was its retrospective nature. When charts completed by others are reviewed, it is not always possible to keep time periods constant, nor to relate laboratory values to time of therapy. It is possible that abnormal electrolyte concentrations may have been present, but escaped detection. The present study was devised to evaluate immediate electrolyte changes by drawing blood for analysis in the emergency room before any supportive therapy was given. The hemoglobin and electrolyte values and the hematocrit readings reported in the patients in this communication substantiate Fuller's findings and support the hypothesis that man and animals react similarly to aspiration of sublethal volumes of water. Although there may be some very early electrolyte changes, as noted in animal studies, fluid and electrolyte homeostasis is reestablished rapidly in patients that survive the acute immersion episode. When the patients arrived at the hospital, serum electrolyte concentrations were usually normal after fresh

water aspiration. Although there was still a mild elevation of sodium and chloride in some sea water victims, the levels were not life threatening, and emergency correction was not necessary. It is probable that patients who aspirate larger quantities of fresh water, sufficient to cause profound electrolyte changes, succumb to the combined effects of these changes, asphyxia, and possibly ventricular fibrillation at the scene of the tragedy. In the case of drowning in sea water, fibrillation is unlikely, and it is primarily the acute asphyxia (possibly superimposed on electrolyte imbalance) that leads to the patient's death.

The delayed decrease in the hemoglobin concentration and hematocrit reading noted in three of the fresh water near-drowning victims in this study deserves further discussion. When sufficient quantities of fresh water are absorbed rapidly into the circulation, hemolysis takes place; however, the degree is not evident from the initial whole-blood hemoglobin concentration and hematocrit reading of near-drowning victims. The explanation for this is evident when one considers that the cyanmethemoglobin method depends upon the hemolysis of cells and subsequent optical transmission for determination of hemoglobin concentrations. Thus, it measures total hemoglobin rather than that in the cell. If hypotonic fluid is transfused into the blood stream via the lungs, the red blood cells may be expected to increase in size, and, although some may rupture, the remaining cells occupy more space than normal and give a high hematocrit reading. It is not until free plasma hemoglobin is excreted and isotonic conditions are reestablished in the blood stream, that the magnitude of red blood cell destruction can be evaluated by these methods.

The blood gas values observed in the patients in this study clearly indicate that the most severe problem confronting the physician in the immediate treatment of the near-drowning victim is acute ventilatory insufficiency with arterial hypoxemia and acidosis. These observations are supported by laboratory studies in which acute asphyxia with persistent arterial hypoxemia and acidosis have been shown to occur in dogs even after aspiration of small quantities (1 ml/lb of body weight) of fresh water and sea water. Halmagyi and Colebatch have demonstrated similar changes in sheep, in which they also found a fall in lung compliance after aspiration of 1 ml/kg of body weight of fresh water or sea water. They interpreted the arterial desaturation of hemoglobin which occurred following aspiration to represent an increase in the portion of cardiac output which was shunted through nonventilated alveoli. With the use of 100 percent oxygen and intermittent positive pressure ventilation (IPPV), normal arterial oxygen saturation could be restored in their animals after aspiration of small quantities of either type of water. The effectiveness of this therapy was only temporary, however, in the animals who aspirated sea water.

The fact that the patients in this study had a large alveolar-arterial oxygen gradient ($A-aDO_2$) when breathing 100 percent oxygen suggests that perfusion of nonventilated alveoli is a major factor in the production of arterial hypoxemia in the acute stages of human near-drowning. Local parasympathetic reflexes may play an initial role in this syndrome after fresh water aspiration. It is doubtful, however, that this mechanism alone is responsible for the long delay in return to normal of ventilation-perfusion ratios since continuous inflation by IPPV with large tidal volumes can return the $A-aDO_2$ to normal. Another factor which more probably contributes to the sustained nonventilation of alveoli is the destruction or alteration of normal surfactant activity which occurs after fresh water aspiration. This then alters the stability of the affected alveoli and makes spontaneous reinflation more difficult. Sea water, although it may physically wash out surfactant, does not alter its surface activity characteristics. It does, however, draw fluid from the circulatory system into the alveoli, and thus the nonventilation of alveoli subsequent to sea water aspiration may be secondary to mechanical obstruction from the fluid itself.

The shunt due to perfusion of nonventilated alveoli was found to persist for approximately 24 to 40 hours. Either the alveoli were reexpanded by then or the perfusion to these areas had ceased. After $A-aDO_2$ has returned to normal when the patient is breathing 100 percent oxygen, a persistent arterial hypoxemia can sometimes be demonstrated for days after the immersion episode in patients breathing room air. This delayed return to normal Pao_2 values may be due to hypoventilation of alveoli (low Va/Q) or to alteration of the normal characteristics of the alveoli and alveolar capillary interphase with production of diffusion problems. Thus, the acute problem is primarily that of alteration of ventilation-perfusion ratios due to perfused, but nonventilated alveoli (ie, intrapulmonary shunts), whereas, the continuing problem following near-drowning most likely is the response of the lung to chemical irritation, ie, aspiration pneumonitis. Studies are currently underway

in the laboratory to investigate these factors. If we assume that these interpretations are correct, it is possible to propose a rational therapeutic regimen for near-drowning victims.

Therapy.—The prime objective of emergency therapy for the near-drowning victim should be to restore normal arterial blood gas and acid-base levels by effective ventilation, oxygenation, and buffers or bicarbonate. If the victim is apneic when rescued, treatment should begin in the water with mouth-to-mouth ventilation. As soon as possible this should be replaced by a method of IPPV capable of supplying maximum oxygen concentrations. Since metabolic acidosis almost invariably accompanies hypoxia in these patients, empirical use of intravenous sodium bicarbonate seems justified. The patient's condition should be evaluated by determination of arterial pH, Po_2, and Pco_2 as soon as possible. Further bicarbonate administration and the extent of ventilatory support and inspired oxygen concentration necessary to prevent further hypoxia will be determined by these values. Active measures should be taken to reinflate atelectatic alveoli by periodic hyperinflation with positive pressure. Isoproterenol may be helpful in reducing bronchospasm secondary to the aspiration of fluid. The patient should also be treated for aspiration pneumonitis at this time by administration of steroids and antibiotics. The patient's progress in regard to reestablishment of normal ventilation-perfusion ratios and adequate oxygenation may then be followed by serial arterial blood gas determinations. Once the shunt through atelectatic alveoli has subsided, it is frequently still necessary to supply the patient with an oxygen-enriched atmosphere. Since prolonged exposure to high concentrations of oxygen may cause extensive pulmonary damage, the inspired concentration of oxygen should be reduced as soon as normal arterial Po_2 values can be obtained with lesser concentrations.

Consciousness at the time of admission is not synonymous with recovery in all patients. One of the two patients who died in this series was the only patient who was not initially apneic or unconscious. His death most probably was due to inadequate pulmonary therapy resulting in profound hypoxia. A similar case has been reported previously by Wong and Grace.

The course of the second patient who died in this series (case six) demonstrates that even with intensive pulmonary care, sufficient destruction of pulmonary tissue may occur to limit the chances of survival. It is also not possible to separate the effect of exposure of the lung to high oxygen tensions from the lesion due to drowning in this patient. Discussion of the relative importance of each is purely academic, however, since she could not be kept alive with lower concentrations. For such patients, future hope may lie in long-term pulmonary bypass support in order to maintain normal Pao_2 values while lung tissues are severely damaged. If the patient's blood can be artificially oxygenated for long periods of time, it is possible that the lung lesion may heal.

When the patient's ventilation and oxygenation are under control, the hemoglobin value, hematocrit reading, electrolyte concentration, and blood volume should be determined. The severity of the residual abnormality in fluid and electrolyte balance will vary with the composition and volume of water aspirated by each patient. For patients that have been resuscitated after aspiration of large quantities of sea water, blood volume replacement (particularly of plasma) must be considered. In patients resuscitated after aspiration of massive quantities of fresh water, there may be sufficient hemolysis to compromise the oxygen carrying capacity of the blood. These patients will benefit from transfusion of packed red cells or whole blood or both. Renal effects of hemolysis are rarely a problem following fresh water near-drowning, as plasma hemoglobin levels of 500 mg/100 ml have been tolerated under these conditions without apparent renal damage. Digitalization, forced diuresis, and induced hypothermia may be considered for selected patients. There is insufficient evidence to support the routine administration of hypertonic salt solution and exchange transfusions to fresh water drowning victims, or hypotonic solutions to sea water victims. Rather it is advisable to evaluate each patient's fluid and electrolyte balance individually and treat appropriately.

This study was supported by Public Health Service research career award GB–33840 and grants GM-12154 from the National Institute of General Medical Sciences and FR–5363 from the Division of Research Facilities and Resources.

B. C. Ruiz, A. V. Showers, RN, and E. J. Newby provided technical assistance, and the house officers of the departments of anesthesiology, pediatrics, and internal medicine assisted in caring for the patients.

(The omitted figure and references may be seen in the original article.)

MEDICAL ABSTRACTS

PATHOGENESIS AND PHYSIOPATHOLOGY OF CYSTIC FIBROSIS OF THE PANCREAS

P. A. di Sant'Agnese, MD ScD (Med), and R. C. Talamo, MD, New Eng J Med 277(24):1287–1293, Dec 14, 1967.

Cystic fibrosis of the pancreas is the most recently recognized of the major chronic diseases of man. Reported for the first time by Fanconi in Switzerland in 1936, fibrocystic disease of the pancreas was not recognized as a separate and distinct disorder until the extensive work of Dorothy Andersen in New York in 1938 and the simultaneous reports of Blackfan and May in Boston and Harper in Australia. Previously, patients with this disease had succumbed either to bronchopneumonia in infancy, so common in the preantibiotic era, or to malnutrition, but the underlying basic condition had not been recognized.

In the present article it is not proposed to duplicate material already at hand but rather to supplement and examine critically present information on the pathogenesis of cystic fibrosis and certain aspects of the physiopathology and immunology of this complex disease. Clinical picture, diagnosis, prognosis and treatment are not discussed.

SMALL-BOWEL ULCERATION—IATROGENIC OR MULTIFACTORIAL ORIGIN?

D. M. Wayte, MAJ RAMC, and E. B. Helwig, MD, Amer J Clin Path 49(1):26–40, Jan 1968.

Fifty-nine cases of nonspecific ulceration of the small intestine are presented from the files of the Armed Forces Institute of Pathology. Eighteen patients gave a history of ingestion of enteric-coated hydrochlorothiazide and potassium chloride.

The clinical and pathologic features are presented, and the role of potassium chloride in the causation of the ulcers has been reviewed and discussed. The authors were unable to differentiate, either grossly or histologically, a so-called potassium chloride ulcer from the more common cicatrizing nonspecific ulcer.

Cardiovascular disease and hypertension were common findings in this series of patients, and it was considered that ischemia may play an important role in ulcer histogenesis. It is possible that in certain patients potassium chloride, instead of acting as a primary and independent agent, may constitute a final escharotic insult to an intestinal mucosa whose vascular supply is already compromised.

DIABETES MELLITUS

Moderators: J. Brown, MD, and B. R. Straatsma, MD, Ann Intern Med 68(3):634–661, Mar 1968.

The cause of diabetes mellitus in man is still uncertain. Theories of etiology have gone full circle, starting from pancreatic disease to absence of consistent pancreatic pathology to demonstration of normal amounts of insulin in adult-onset diabetes, and now to relative insulin deficiency. It is now accepted that a long period of prediabetes precedes the onset of hyperglycemia or glucose intolerance, the latter often appearing incident to a metabolic stress such as obesity, infection, pregnancy, or corticosteroid or growth hormone excess.

Renal disease in diabetes may be the cause of death in one half of juvenile-onset cases and consists of four types of glomerular lesions: nodular, diffuse, "fibrin cap," and "capsular drop." Diffuse or nodular lesions, or both, are found in almost all diabetics with clinical evidence of renal disease; the condition is usually progressive. There is a direct correlation between the severity of the diffuse glomerular lesion and clinical renal disease—proteinuria, impaired renal function, hypertension, and nephrotic syndrome.

Diabetic retinopathy is best considered as a syndrome, characterized in its full-blown form by angiopathy, exudates, proliferative changes, and vitreous hemorrhages. This condition is present to some degree in approximately half the patients with diabetes mellitus. The course of diabetic retinopathy is variable, and the prognosis is therefore difficult to determine, but a substantial percentage of the patients eventually develop vision impairment from diabetic retinopathy. Thus, it constitutes one of the leading problems, if not the leading problem, in ophthalmology today.

In terms of management, every effort should be made to prevent retinopathy by giving the patient the benefit of careful and continuing medical management. When the problems of diabetic retinopathy do develop, there are several methods of therapy that are now used—selectively, cautiously, and with an awareness that there is still much to be learned about this disorder and about its response to treatment.

DENTAL SECTION

DENTAL APPOINTMENTS

CAPT H. R. Superko, DC USN.

In order to fully utilize its capabilities and attain a maximum effectiveness, a Dental Activity must have an appointment system which will accomplish several objectives:

First: It must locate and define the dental problems of Navy Personnel.

Second: It must provide a system to assign priority treatment for individuals and for conditions which are most urgent.

Third: It must effectively keep a patient in each operator's chair without requiring long periods of patient delay in our Waiting Rooms.

The following is a detailed account of how these objectives are met at one activity whose primary mission is to service units of the fleet. It may appear that unneccessary attention is paid to small details and thus look complicated. In actuality, it is the small details that make it simple and effective. That there is no lost time in the operatories is not remarkable but there are almost no man hours lost by shipboard personnel in our Waiting Room. This, in itself, is a dividend much appreciated by the patient and by his Commanding Officer who wants him working aboard ship.

The key to this system is to appoint a dental technician as a liaison for each group scheduled. This is not a full-time job but assures a uniform and prompt action when required. As each group is scheduled (in our case usually a ship's crew) a duplicate of the pay list is obtained from the ship's Finance Officer. Either the ship's Medical Representative, our technician or both, note on this list, the dental classification of each man as indicated by his color coding. Also noted is the date of his last dental examination. If six months or less, he is not re-examined but is appointed for treatment on his existing classification. If his last examination was not that recent, he is scheduled with a small group to appear for new bitewings, examinations and classification by a dental officer. At this same time, his group is given a preventive dentistry lecture and stannous fluoride treatment by dental technicians. As the dental officer charts each patient, he indicates by a small red check those conditions which require immediate treatment. Those that he does not red check are considered to be arrested caries or an elective procedure not requiring priority. These conditions may or may not be treated as time and manpower permits. The dental officer also notes in pencil on the 603 the number of chair hours required to effectively treat all red checked conditions. It has been found that one dental officer and four technicians can examine sixty-five patients each morning. This means bitewings, lectures and stannous fluoride treatments and an appointment schedule for each. Appointments are made by a technician who notes the number of hours required as penciled in by the dental officer. He assigns patients to operatories that will be available, as indicated by a blank schedule of available officers and hours provided by the Clinic Director. The technician who makes these appointments also notes on ship's roster (from the pay list), the newest dental classification just determined by the dental officer's examination. This information will be used to help judge our final effectiveness. We are now assured that each man has been evaluated and assigned priority treatment as indicated to be necessary.

At this point we realize that many of these patients may not keep the appointments and steps must be taken to insure that they will. Appointments are broken for many reasons: last minute job assignments, transportation problems, some forget and some would rather go to the gedunk. Most of these are controllable and, in all cases, patients can be prompted to keep the appointment or a substitute can be provided rapidly. This is where the liaison man is effective. Naturally, the Commanding Officer of the ship's crew or the group has been made thoroughly aware of the program and gives it his full support. No trouble has ever been encountered here.

Our liaison man sees that each day's appointments are published in the ship's Plan-of-the-Day. This reminds the patient and his Division Officer in time to plan the day's work. In addition, our man pulls the 603's from the ship's records and gives them to each Division Officer to give to the patients. This is double insurance that the Division Officer is aware of where his man will be and the man himself considers the appointment more in the nature of an order rather than an option. Our liaison man who boards each ship early determines by muster time, if any of his scheduled patients are not present or for any legitimate reason cannot keep his appoint-

ment. He immediately procures a substitute from the color coded records on board and reappoints the first patient as his availability permits.

Our liaison man leaves the ship as soon as his 603's are in the Division Officer's hands and it appears that all scheduled will present themselves.

In all cases the Commanding Officer of the group is kept informed of those who fail or are late and the crew quickly gets the word that most Commanding Officers consider this a Mast Offense with no one caring to repeat.

For those in each group who may have been on leave—ill or for some reason missed the program, provision is made to locate and render treatment. To locate, the Liaison Agent at the end of the scheduled program, again uses his master pay list and marks in the latest dental classification as obtained from the color coded charts. It is a simple matter to determine any personnel who remain in Classes III, IV, V and to provide appointments for them.

With this or a similar method of locating the most needy patients, and assuring priority treatment, over 90% of the personnel are put in Class I or II by the end of the program. With the additional effort to locate and appoint stragglers, the 100 percent mark is often approached.

To complete the program, the commanding officer of each group receives the statistics of what was accomplished for his crew. In all cases, a short briefing before the program starts and a summary of conditions prior and subsequent to treatment has resulted in excellent cooperation and helped make the program effective.

It is not presumed that every dental activity should operate identically to the one outlined but it is contended that the three basic principles of an appointment system should be the same. Local conditions will dictate variations but the objectives will be to provide the maximum of essential treatment to those personnel most essential to naval operations.

The following is a representative report of dental care accomplished utilizing the system described above:

U.S.S. BRUMBY (DE 1044) STARTED PROGRAM: 3 JANUARY 1968

185—Patients examined at pier facility.
* 6—Patients not appointed due to leave.
6—Patients transferred prior to receiving treatment.

173—Patients completed program.

	CLASSIFICATION IN FILES BEFORE EXAMINATION	CLASSIFICATION AT EXAMINATION	CLASSIFICATION AFTER TREATMENT
CLASS I	95 (54.9%)	46 (26.6%)	136 (78.6%)
CLASS II	55 (31.7%)	81 (46.8%)	29 (16.7%)
CLASS III	21 (12.1%)	39 (22.5%)	1 (00.5%)
CLASS IV	2 (01.3%)	5 (02.8%)	7 (04.2%)
CLASS V	0	2 (01.3%)	0
TOTALS	173 =100.0%	173 =100.0%	173 =100.0%

95.3% of all patients completing program in Class I or Class II.
All Class IV patients have completed operative dentistry phase of their treatment, thus, as concerned with operative dentistry, 99.5% of the patients are in Class I or Class II.
*—Undergoing treatment after compilation of Data.

THE LONELIEST MAN

Defense Management Journal, Vol. 1, Issue 1, page 31, Winter 1967–68.

In a recent article entitled, "The Loneliest Man in the Military is the Man With a New Idea," Doctor Charles F. Austin, Professor of Organizational Behavior and Business Administration, The American University, makes a devastating point of interest to Navy personnel.

He says, "An eminent university professor after much research has determined that over half of all good ideas that reach fruition are turned down six times before they are adopted. The question that can't possibly be answered with an honest 'yes' is: Do the military personnel in your organization feel free to press on with an idea through six successive rejections?"

A letter from a recently released junior dental officer bore this out, at least in a pair of instances. His first senior dental officer commenced his indoctrination lecture with the statement that everyone would do things his way or be court-martialed.

His successor had no problems, "He simply said, 'No,' to everything."

Frequently in these columns well tried ideas are presented, particularly in the area of handling people—enlisted, junior officers and patients. The question is, are some of these ideas receiving consideration and fair trial or do we complacently say, "No", six times in the knowledge that our activities are above and beyond improvement?

Thus, it is axiomatic that we should not reject a new idea without first being willing to give it full consideration or a fair trial.

s/F. M. Kyes
Rear Admiral, DC, USN
Assistant Chief of the Bureau of
Medicine and Surgery (Dentistry)
and Chief, Dental Division

PERSONNEL AND PROFESSIONAL NOTES

SEMINAR—COMMANDING OFFICERS OF NAVAL RESERVE DENTAL COMPANIES AND APPROPRIATE DUTY DENTAL OFFICERS

A Seminar for Reserve dental officers from the First, Third, Fourth, Fifth, Sixth, and Ninth Naval Districts was held at the Bureau of Medicine and Surgery, Washington, D.C., during the period of 11–15 March 1968.

The purpose of the Seminar was to provide indoctrination and orientation in the organization, administration and operation of the U.S. Naval Dental Corps from the Bureau level, and to acquaint the trainee with the current concepts and trends which affect the U.S. Naval Dental Corps' Reserve Program.

District commandants issued orders to Naval Reserve Dental Company commanding officers, executive officers or their representatives who had not attended such a Seminar in the last two years and who have a mobilization assignment.

Following a day's briefing by RADM F. M. Kyes, DC USN, and his staff at the Bureau of Medicine and Surgery, the officers visited the following activities in the Washington area: Bureau of Naval Personnel, Marine Corps Development and Education Command, Armed Forces Radiobiology Research Institute, Naval Dental School, Naval Medical Research Institute, Armed Forces Institute of Pathology and the District of Columbia Dental Society's Annual Meeting. CAPT Robert F. Tuck, DC USNR, was chairman of the Seminar.

All officers who attended the Seminar will be considered as having completed part of their regular two-week active duty for training.

OCCUPATIONAL MEDICINE SECTION

INDUSTRIAL HYGIENE FOR INSULATION WORKERS

J. LeRoy Balzer, MS, Berkeley, Calif., JOM 10(1):25–31, January 1968.

The use of asbestos in the United States and the world has increased substantially since the early Nineteen Thirties. Among the occupationally exposed, the use of asbestos has resulted in many cases of disabling pneumoconiosis, known as asbestosis. Epidemiological evidence also shows that persons occupationally exposed have a higher incidence of malignancies of the lungs, pleura and peritoneum. Even though the first cases of asbestosis were recognized among textile workers in the early Nineteen Hundred's, Ellman was the first investigator to identify specifically the disease in the insulating worker.

Fleischer et al. found few cases of asbestosis among the insulation workers in the eastern Navy shipyards, they minimized the potential hazard, as the dust levels were below the recommended standard. Marr, working in Southern California shipyards, further identified the environmental hazards associated with insulating materials containing asbestos. The purpose of our research is to describe the incidence of pneumoconiosis and malignancies among

the insulating workers in the San Francisco Bay Area and to make observations and measurements of his working environment. This paper summarizes the preliminary environmental findings.

Union membership: The men who apply insulation materials first organized in New York City as the Salamanders Association of Boiler and Pipe Felters in 1884, and were later rechartered by the AFL in 1910 as The International Association of Heat and Frost Insulation and Asbestos Workers. San Francisco Local 16 is a member of the international union and has a membership of approximately 500 men encompassing the geographical areas of Northern California and Northern Nevada. Over 40% of the members have been in the trade for over 20 years and 70% for over 10 years. The members of this union are primarily employed by the building trades; however, at various times the shipyards demand an increased number of men, such as during World War II. In general, insulators who are employed by the U.S. Naval Shipyards have their membership outside of Local 16.

The uniqueness of this trade is that there are very few specialists; each man can do any insulating job required of him. He may be called upon to work with any one of 50 different products. The only specialization is that some men prefer heavy construction to marine construction and repair, or commercial building. Thus, they may choose to work for one contractor specializing in a particular area. As an example of areas of work preference, 380 active members were surveyed and found employed, on a typical work day during the summer of 1967, in the following three major work areas: 220 men in heavy industrial construction, 100 in commercial building and 60 in marine construction and repair.

Insulating products: Analysis of the materials used by the contractors in the San Francisco Bay Area has been made by on-site evaluation, laboratory analysis, and contacts with salesmen, distributors and contractors. This survey has indicated that fibrous materials (glass and asbestos-containing products) account for 90% by volume of the materials used. The other 10% of the materials are adhesives, corks, foams, glass, polystyrenes, and polyurethanes.

Asbestos materials: The insulator spends approximately 45% of his time working with these materials. Table I summarizes the approximate amounts and types of asbestos fibers used locally in 14 different asbestos-insulating products, manufactured by seven major producers of insulating materials in the United States.

The stated types of asbestos fibers in seven of the materials were confirmed by x-ray diffraction analysis using a Norelco x-ray unit equipped with a copper target and x-ray diffraction tube.

Asbestos, as used by the insulating industry, consists mainly of chrysotile, a magnesium silicate mined principally in Canada, and amosite, an iron magnesium silicate mined in South Africa. Since World War II, amosite has been the most widely used fiber in insulating materials. However, Table I shows that the use of chrysotile has increased to where the two are presently in about the same number of insulating products.

Asbestos is usually combined with a filler material such as calcium silicate, in the amounts indicated in Table I, and pre-formed into various shapes to be used as insulating materials. Until recently, magnesium silicate was often used, but execpt for some in warehouse stock and a few special orders almost all the new silicate-containing insulating materials are made of calcium silicate. In addition, perlite and other materials are used as binders in manufacturing insulating products.

Manufacturers of asbestos insulating materials use varying amounts and types of asbestos fibers in their products and may rebrand their product for distribution by another manufacturer. Contractors will order specific types of insulation because of their thermal properties, disregarding the type of asbestos fibers they contain. These practices on the part of the manufacturers and contractors make it impossible to reconstruct, for environmental evalu-

Table 1.—Type and Percent of Asbestos in Insulating Products Used in the San Francisco Bay Area

Type of Asbestos	% by Weight	No. Products
Chrysotile	10– 15	2
Chrysotile	85–100	3
Amosite-chrysotile	10– 15	3
Amosite	10– 15	3
Amosite	95–100	3

ation purposes, a working population that has a "pure" exposure to one type of asbestos fiber.

Fibrous glass: The insulator works with fibrous glass about 45% of his time. These glass fibers are made of mixtures of silicon dioxide, oxides of aluminum, calcium, magnesium, boron and other additives. In general, the fibers of most commercial insulating products have a mean diameter of 4 microns or greater. The fibers are bonded together by a water-based phenolic resin and cured. During or after the curing, the glass blankets are formed into the appropriate materials: for example, pipe coverings and blocks.

In our laboratory, we have optically determined the diameter in microns of various samples of fibrous glass insulating materials used in our area. The acoustical materials have the largest diameter, 11 to 14 microns; the building and duct insulation, 4 to 7 microns; pipe covering, 4 to 6 microns; and the special high temperature material, 1 to 2 microns.

Adhesives and coatings: In general, the type and percent of solvents used in the adhesives and coating products were obtained from the manufacturer representatives or technical data sheets. There are nineteen products used in the Bay Area accounting for 90% of the materials applied. They contain the following solvents: aliphatic hydrocarbons (naphtha, hexane and other petroleum distillates), ketones, aromatic hydrocarbons (xylol and toluol), chlorinated hydrocarbons (methylene chloride, trichloroethylene, and perchloroethylene), and isopropyl alcohol. These materials are used by the insulator 5% of his time. The solvents are in combination with a number of plastics, organic and rubber resins, and paraffins.

The use of these solvents can be divided into two groups: those containing from 1% to 10%, and those 10% to 95% by weight. The first group generally contains the alcohols and aromatic hydrocarbons while the second group the chlorinated and aliphatic hydrocarbons. The latter group constitutes the majority of the nineteen products used in the Bay Area.

Other: This group contains the remaining materials that the insulator uses. Foam glass materials are a mixture of glass chips (greater than 10 microns in diameter) expanded by hydrogen sulfide gas into block forms. This product, along with cork and rubber materials, is mainly used for refrigeration insulation. Polystyrenes are being used in an ever-increasing amount, especially in the area of cryogenics. Polyurethanes, at present are not being used because of a lack of adequately trained personnel.

Environmental survey: The insulator is exposed to a multitude of materials and environmental stresses. To obtain a "classical" time-weighted exposure for this trade for every one of these conditions is impossible; however, it is possible to present data that will indicate the variability of these exposures. In contrast to other occupational groups who generally stay in the same working environment, the insulator is in a continuously changing environment; the work locations, materials, position, humidity, temperature, ventilation, noise levels, and other variables are in a state of flux. Environmental exposures to the insulator also result from the trades around him, such as welders, painters and fireproofers. In order to better describe the work environment, the jobs performed by the insulating worker have been divided into six areas: (1) Prefabrication: (10% of his time) materials are pre-cut and shaped using hand or power saws; (2) application: (40% of his time) materials are fitted, hammered, or carved, and attached to the surface by wiring or gluing; (3) finishing: (30% of his time) materials are coated with asbestos containing cements, resins, asbestos or cotton cloth, or petroleum-based sealers; (4) tearing out: (10% of his time) removal of old or unusable materials in the process of insulating or reinsulating; (5) mixing: (5% of his time) mineral wool, asbestos, fibrous glass, and cements are mixed separately or in combination in buckets or troughs; and (6) general: (5% of his time) cleaning up of old insulation, transporting of materials.

Dust exposures: The environmental sampling for dust exposures has been limited to areas in which asbestos-containing materials were being applied.

In order to compare the environmental sampling data with past studies of shipyards and textile mills, one set of samples was taken using the midget impinger. Results of these samples are summarized in Table II. The data represents both breathing zone and general air samples. The standard method of counting prescribed by the American Conference of Governmental Industrial Hygienists (ACGIH) was used and both fibers and grains are pooled in the total count.

As can be seen from Table II, the areas with the highest dust concentrations and exceeding the present TLV are prefabrication, tearing out, and mixing. However, these three areas account for less than 35% of the man's working time when applying asbestos materials.

Table 2.—Midget Impinger Counts by Job Classification*

Million Particles per Cubic Foot

Job Classification	*Mean Count*	*Range*
Prefabrication	7.0	0.85–32.0
Application	3.8	0.85– 9.0
Finishing	2.8	1.4 – 6.9
Tearing Out	5.9	2.8 – 9.0
Mixing	8.7	3.3 –18.0
General	1.6	0.5 – 3.4

*Adapted from the author's graph.

Since most investigators doing research in the pathogenesis of asbestos suggest that the fibers play an important part in the disease process, a major emphasis was placed on obtaining fiber concentrations under various working conditions.

The membrane filter has proved successful in evaluating the environmental exposure to fibrous materials. The membrane filter samples were collected using a millipore type AA filters in field monitor cases and connected to personal air samplers and attached to the workers for periods ranging from 30 minutes to 2 hours. The fibers were counted by clearing a wedge-shaped segment of the filter using a modified technique of the USPHS at 430-X magnification using phase contrast illumination.

Timbrell's criteria for respirable fibers (diameter smaller than 3.5 microns) was used for classification purposes. His experimental work shows that respirability is dependent on diameter, not length. An aspect ratio (length to width) of 3:1 was used for differentiating between a fiber and a grain. Depending on the working conditions, 98% ±2% of the fibers counted fall into this respirable category.

Solvent exposures: Only a small number of measurements have been made using a Kitagawa detector kit and a combustible gas indicator for aromatic hydrocarbons. At present no readings have approached the TLV for the solvents listed. However, since there are often welders operating in the same area, there is some concern about the decomposition products from chlorinated hydrocarbons, i.e., phosgene and hydrogen chloride. Additional field sampling for solvent exposures is contemplated especially in areas where men are working under confined conditions, for example, in ships, ventilator shafts, etc.

Temperature and humidity: Another condition that affects most of the workers is the extreme temperatures and humidity. In the commercial and heavy industrial building groups the humidity measurements ranged from 20 to 100% with temperature ranges of 32° to 110° F. The marine construction and repair group experience the most extreme conditions, although the ranges of temperatures would compare with the other groups. The extremes measured on one of the jobs were 95% humidity and 95° F.

Noise: Sound level measurements have been made using a general radio type 1551–A sound level meter. In general, few areas have sustained readings above 90 d.b. However, if chippers, caulkers, riveters, and grinders are being used in the same area, readings above 100 d.b. are not uncommon. These specific short-time exposures need further study, specifically octave-band analysis. The present sound level data shows a general agreement of readings between the Broad Band Network and the C-Band Network in general work areas when only small grinders and stud welding guns are being used.

Discussion

Anyone looking at the present basis for the threshold limit value (TLV) or 5 mppcf as recommended by the American Conference of Governmental Industrial Hygienists (ACGIH) in 1946 realizes that it is not based on solid evidence. The method used in setting the standard includes all dusts (both grains and fibers); and a large portion of the asbestos fibers that were collected had a diameter, when viewed at 100–X magnification, well below the resolving power of the light microscope.

Recognizing these inherent errors, most industrial hygienists have used the impinger count as an indirect measure of dust control and until recently thought that dust counts averaging below 5 mppcf would control the incidence of asbestosis. Cooper, in his reviews of recent epidemiological studies regarding the incidence of asbestosis and its relationship to the present threshold limit value (TLV),

makes it very clear that this supposition is no longer true. Our own studies of the insulation workers in the Bay Area also show over-all environmental dust counts to be below the TLV; however, definite radiologic changes have been observed in our Asbestos Union population. These observations indicate that the present time-weighted average of 5 mppcf for asbestos is not preventing asbestosis. The better asbestos industries, by reducing dust counts well below the TLV, have shown to their satisfaction and others a decreased incidence of asbestosis. However, even with the reduced exposures, the malignancy question has not been answered.

Asbestosis in the insulating worker can be prevented by instituting the following: total work enclosures, exhaust and forced air ventilation of dusty areas, personal respiratory protection, changes in work habits, and substitution of materials. All of these preventive measures cannot be adopted immediately and are all not applicable to every job. The industry must adopt some of these changes in order to reduce the environmental dust exposures and, thereby, extend the working life of the insulator.

Prefabrication of materials should be done in an open-end booth with exhaust fans, such as the spray paint booth. This will substantially reduce the operator's dust exposure. The mixing of muds should also be enclosed in a booth and an automatic mixer be utilized, thereby controlling dust levels that occur when these materials are mixed in open areas. This operation could also be done in central areas and trucked to the job since many of the materials do not dry out if they are kept tightly covered.

The use of local exhaust and forced air fans in the work area and on certain equipment, i.e., saws, will also reduce dust exposures. It is also realized that this is impractical on some jobs because few men work in one area long enough to justify the setting up of an elaborate ventilation system. However, when large boiler and generator jobs are in process, local exhaust or forced air fan systems should be used. This type of system could also be used to cool the men in areas of extreme temperature and humidity, such as in marine construction and repair.

The use of personal respiratory equipment is very important, but what is more important is the development of a mask that has a filter with a low resistance to air flow and a face piece that is easily fitted to the man and wearable. Most of the present masks do not fit properly and the filters, besides having a high resistance to flow, clog very quickly. This makes it necessary to change the filter frequently, or as is most often the case the men simply remove the mask and continue to work. Another form of respiratory equipment is the supplied air respirator which should supply enough air to cool the man as well as meet his physiologic needs. This requires elaborate hose and compressor systems and is seldom economically feasible or desirable. But it is suggested that personal air supplied respirators with their own power units be used in areas of high dust exposure such as prefabrication and tearing out. Appropriate respiratory protection should also be made available for use in areas where high solvent concentrations exist.

Changes in work practices such as the use of a water spray to wet down some materials before they are cut would substantially reduce the dust exposure. Industrial vacuum sweepers could be used for clean-up instead of brooms, thus reducing the dust level. In addition, tearing out of old insulation could be done with local exhaust hoses connected to a vacuum sweeper. All these steps would reduce the present high levels of dust exposure at these various jobs. Mixing of muds in closed plastic bags has also been suggested and tried, but data on acceptability is presently not available.

Substitution of new materials such as fibrous glass is possible under certain conditions, but at present we do not know enough about the physiologic effects of fibrous glass to suggest the total change to this product. When proposing the substitution of new materials to replace asbestos, the engineers often have reasons, too, for not changing these materials. Asbestos, they feel, is the only product that will withstand the day-to-day impact of man, weather, and machines without adding some additional protective covering, such as metal. Thus, at present for the marine construction and heavy industrial insulation jobs, there is no economical or desirable substitute for asbestos insulation products. In fact, the use of asbestos-containing insulating materials in the Bay Area is on the increase in heavy industrial construction.

Summary

The asbestos worker is exposed to amosite and chrysotile asbestos-containing materials, fibrous glass, cork, plastics, and adhesives. Working in industrial and commercial building projects and marine construction and repair, he is exposed to many other environmental hazards not created by his own trade.

Although he works with asbestos-containing products 45% of the time, the over-all time-weighted average exposure to asbestos-containing materials is below the presently recognized TLV of 5 mpccf. The three work areas in which the dust levels were above the TLV (prefabrication, tearing out, and mixing) account for less than 20% of his total work time. However, the incidence of radiographic changes indicative of asbestosis is over 25% in our men with 20 years or more of work. This and other evidence suggests that the present TLV is too high.

Incidence of asbestosis and the risk of malignancies in the asbestos worker can be reduced by local and general ventilation, substitution of materials, changes in work habits and personal respiratory protection combined with education of the men to reduce their own exposures to asbestos-containing dusts.

(The references may be seen in the original article.)

PROGRESS IN DETECTING THE WORKER HYPERSUSCEPTIBLE TO INDUSTRIAL CHEMICALS

H. E. Stokinger, PhD and J. T. Mountain, MS, Cincinnati, Ohio, JOM 9(11): 537–542, Nov 1967.

As everyone familiar with industrial standards knows, the threshold limit values for the control of industrial atmospheres are designed to protect "nearly all workers" from industrial diseases. This "partial protection" clause has been a cause of great concern to the Committee on Threshold Limits because of the Committee's inability, until recently, to find a means of minimizing this defect. Workers not so protected comprise, by and large, a small minority of individuals hypersusceptible to, or abnormally predisposed to industrial chemicals. However, medical advances in the last few years have revealed ways of identifying those presently not fully covered by the threshold limits.

It is becoming generally recognized by the medical profession that the great preponderance of hypersensitive responses seen among industrial workers are attributable to altered genetic patterns of metabolism. Stanbury et al. have assembled and discussed more than 120 such hereditary diseases based on inborn errors of metabolism; others are continually coming to light.

This report will present and discuss 3 relatively simple tests applicable to the industrial scene for the detection of the hypersusceptible worker. The tests for industrial application evolve in the following way. Since the hypersusceptibility is genetic in origin, one merely subscribes to the unitary hypothesis for which Beadle, Tatum and Lederberg received the Nobel prize in 1958: 1 gene, 1 enzyme system; 1 altered gene, 1 altered enzyme system. Hence the problem of finding an appropriate test merely resolves itself into finding the altered enzyme, or associated factors or products, related to the hypersensitivity. The "finding" is done by keeping abreast of the medical genetic literature.

Tests for Hypersusceptibility

Familial Pulmonary Emphysema and Hereditary Antitrypsin Deficiency—Pulmonary emphysema in man is coming to be recognized as a disease of multiple causation. Its incidence has been attributed to the weather, smoking, chronic bronchitis, alcohol, and certain industrial exposures among other things; it may also develop with apparent spontaneity. Recently, however, evidence, both from abroad and in the United States, indicates that in some instances emphysema may be related to an inherited disorder. This disorder consists of a deficiency of $alpha_1$—antitrypsin, a glycoprotein found in the $alpha_1$—globulin fraction of the serum, that comprises 90% of the total trypsin inhibitory capacity of serum. Loss of this inhibitory capacity makes the alveolar tissue of the lungs vulnerable to proteolytic enzyme attack, which destroys the alveolar walls and leads to emphysema. It seemed to us that the industrial physician would like a simple clinical chemical test to distinguish hereditarily based disease from job-claimed disability.

Pulmonary emphysema of the familial type has certain distinguishing features, according to Talamo et al. Onset is unusually early, commonly the mid '30s; the earliest recorded onset is 27 years. Incidence in females is higher than expected for the

usual forms of emphysema. There is an absence of clinical chronic bronchitis in the early phases, and the emphysema is panlobular. Death often occurs before 55.

Incidence—Determination of the incidence of this condition is fragmentary. Eriksson found 4 homozygotes in 6,995 sera in Sweden, 1 in 1,700 (0.057%), and the frequency of heterozygotes to be 4.7%. Kueppers et al. determined an incidence of 2.1% for heterozygotes among 193 individuals in the state of Georgia, and guessed the homozygote frequency to be 1/10,000 (0.01%). Because the linking of antitrypsin deficiency to pulmonary emphysema is so recent, it is too early to draw conclusions regarding frequency among ethnic or national groups.

Test for Serum Antitrypsin Deficiency—Very simple clinical chemical tests are available for determining the amount of antitrypsin activity in the serum. The semiquantitative procedure of James et al. consists of placing graded amounts of trypsin in marked squares on a used x-ray plate, to which have been added and allowed to react measured amounts of the test serum. After allowing 2 hr. for reaction, the surface of the x-ray plate is rinsed and the size of the hole left by the digested gelatin on the plate is a measure of the antitryptic deficiency. Other more quantitative tests are available.

With specific tests available, the industrial physician is in an advantageous position to decide whether a claimed case of emphysema is job-connected or not. The serum of individuals with hereditary antitrypsin deficiency will not have the capacity to counteract trypsin digestion of the gelatin, and will show a clear spot in the x-ray plate acccording to the rapid screening procedure described by James et al. Hence, we are suggesting this test as a simple means of detecting the hereditarily prone emphysema worker.

The fact that alpha$_1$—Globulin, of which apha$_1$—antitrypsin factor is a part, increases in pancreatitis and in inflammatory processes (respiratory infections) need not concern us, we believe, because in individuals with the hereditary deficiency in antitrypsin factor, the defect affects the rate of production of the factor, rather than causing an alteration in the primary structure of the factor.

Predictive Test for Hypersusceptibility to Hemolytic Chemicals—In the United States, the possibility of using the inborn errors of metabolism to explain the response of the worker hypersusceptible to chemically induced anemia was hinted at by Brieger, Jensen, and Zavon in 1962 and 1963. About this time, Stokinger and Mountain proposed predictive tests for detecting the industrial worker hypersusceptible to hemolytic type chemicals. Noting the similarity of structure of industrial chemicals to that of drugs causing hemolysis, we drew up a list of industrial chemicals to which workers could be expected to be sensitive. This list gives some of the chemicals and drugs from which exposure will predictably result in an abnormal response in the hypersusceptible worker; the list is only suggestive with no pretense of being complete.

Acetanilid
Amyl nitrite
Aniline
Arsenic trioxide
Arsine
Benzene
Benzidine
Carbon tetrachloride
Chlorate
Chlorobenzene
Chloroprene monomer
Cresol
Dinitrobenzene
Dinitrotoluene
Guaiacol
Hydroquinone
Hydroxylamine
Lead
Lead arsenate
Methylcellosolve
Naphthalene
Naphthol
Nitrites
Nitrosamines
P-dichlorobenzene
P-nitrochlorobenzene
P-phenylenediamine
Phenylhydrazine
Phosphorus
Pyrocatechol
Selenium dioxide
Sulfonamides
Tetrachloroethane
Toluidine
Trinitrotoluene
Raised oxygen pressure
Numerous N-containing drugs

Hypersusceptibility tests are useful in predicting the direct, or indirect but additive effects of some of these chemicals, or in distinguishing between effects due to chemical exposure vs. congenital defect. Three such tests were available at the time of compilation; the assay for glucose-6-phosphate dehydrogenase (G-6-PD), the glutathione (GSH) instability test, and the methemoglobin reduction test. All provided various measurement of the degree of defect in the G-6-PD, 1 of the carbohydrate metabolizing enzymes of the red cells. The tests were merely those that had been found valuable in detecting the primaquine-sensitive responders. The key to the industrial application of the test was

the recognition that numerous industrial chemicals possessed toxicologic actions or structures similar to drugs that produced hemolytic crises in sensitive individuals. Hemolytic chemicals utilize and further reduce available hydrogen, already in short supply for needed maintenance of red blood cell membrane integrity, because of deficient action of the enzyme G-6-PD. This inability to maintain sufficient NADPH and glutathione in the reduced state, through insufficient metabolic hydrogen, in some as yet unexplained way causes rupture of the red cell membrane. Without the added stress of exposure to hemolytic chemicals, these sensitive indivudals carry on normally with their reduced metabolic functions of the red cell, without cellular breakdown.

G-6-PD Defect Tests—For screening purposes, where the object is simply to detect the atypical individual, tests relying on visual indicators, i.e., dye decoloration, color development, or fluorescence, are convenient and have been employed for screening industrial populations. Sets of reagents and materials for such tests are available from clinical laboratory suppliers. To avoid the need for maintaining anaerobic conditions, to lessen the time and manipulations involved and to avoid the complications introduced when anemia is involved, Beutler has developed a procedure designed to obviate these difficulties. In his test, normal blood, which readily generates NADPH, yields a spot which fluoresces under long-wave ultraviolet light: the blood-reagent spot from an enzyme-deficient specimen is characterized by failure to do this.

Incidence of G-6-PD Affection—The approximate incidence of the hemolytic defect and its worldwide distribution according to racial subgroup is given in Table 1. From the standpoint of the United States working force, the group most affected is the Negro of African descent, about 12% for males and 9% for females. Sardinians, but not the Ligurian Italians, have equally high rates, as do the Filipinos. Worldwide, the Kurdish Jews have the highest incidence yet found for any group. The low frequency of 1/1000 for the United States probably represents the result of the intermingling of the many groups of varying affection.

Other Applications of G-6-PD Test—The G-6-PD assay is useful in ways other than for detecting the individual hypersusceptible to hemolytic agents.

1. Table 2 shows the responses that are obtained in normal individuals exposed to lead by 3 tests related to the pentose-shunt-metabolism mechanism of the erythrocyte. Exposure to substances such as those listed above might be expected to be registered by G-6-PD assay.

2. Individuals with intermediate defect may hyperreact to a wide variety of household drugs.

Table 1.—Incidence and Distribution of Hemolytic Defect

Race	Subgroup	Incidence (%)
Negro	American (African descent)	12
	Leopoldville	18
	Stanleyville	15
	Nigerian	10
	S. African Bantus	3
Caucasian	American	0.1
	British	0.1
	American Indians	0.0
	Eskimo (Alaskan)	0.0
	Peruvian Indians	0.0
	Carib. Indians	2
	Oyana Indians	16
	Italians (Ligurian)	0.0
	Sardinians	13
	Iranian	8
	Arabs	3
	Jews	
	Kurdish	60
	Persian & Iraqui	25
	Turkish	5
	Yemenite	5
	N. African	2
	Ashkenazi (European)	0.2
Mongolian	Chinese	5
	Japanese	0.0
Malaysian	Filipinos	12
	Micronesians	0.1
	East Indians	11

Table 2.—Comparison of G–6–PD, GSH and GSH– Stability Test in Lead Poisoning

Subjects	G-6-PD units*/10 r.b.c.	GSH mg./100 ml. r.b.c.	GSH after stab. test
Normal	277 ± 12	57 ± 6	47 ± 4
Pb-clinical effects acute and subacute	231 ± 31 $p < 0.01$	40 ± 9 $p < 0.01$	35 ± 10 $p < 0.01$
Pb exposed, no overt symptoms but Pb and coproporphyrin elevated in urine	245 ± 33 $p < 0.05$	47 ± 11 $p < 0.05$	41 ± 8 $p < 0.05$

From Rubino et al. Minerva Med 54:930, 1963.

* Unit = Δ .001 O.D./min.

These persons (the "chronic pill-takers") may constitute a significant part of the "absentees" from protracted response to drug treatment of such things as common colds. Recognition of the basic defect can help the industrial physician decide between job-connected and self-inflicted illness.

3. Fibrotic Lung Disease. A parallelism has been found between the activity of G-6-PD and collagen in newly formed connective tissue. This suggests the use of G-6-PD assay applied to tissue for detecting early fibrotic changes in the lung as a replacement for the more difficult test for collagen.

4. 100% oxygen. At least one case is known where a subject (Negro) after 26 minutes exposure to 100% O_2 at 30 psia developed a hemolytic anemia; blood tests showed this person had the G-6-PD genetically defective red cell.

Status—Since our introduction of testing in 1962 and its publication in 1963, more than 15 industries, research centers, or health-oriented groups are either using the G-6-PD test or have inquired into its use. Industries finding the test useful are the manufacturers of dyes and dye-stuff intermediates, metals, particularly lead, and drugs.

Predictive Test of Carbon Disulfide Response—A clinically useful test has recently been reported by Djuric et al. that not only detects those workers exposed above the U.S.-recommended threshold limit, but is also capable of identifying the hypersusceptible viscose-rayon worker. The test simply utilizes the rate of color disappearance of iodine, in its reduction by sodium azide through the catalytic action of a CS_2 metabolite, in the urine of the exposed worker according to the following reaction:

$$NaN_3 + I_2 \xrightarrow[\text{Catalyst}]{\text{Urinary } CS_2 \text{ metabolite}} 2NaI + 3N_2 \uparrow$$

Color → No color

Simultaneous creatinine determination permits account to be taken of fluctuations in urine volume, and avoids the need for 24-hr. urine specimens. Because the rate of disappearance of the iodine color is not linear, but is related exponentially to the degree of exposure index, E is expressed as $E = C \log t$, where C is the concentration of creatinine in mg./ml. and t is time in seconds to the disappearance of iodine color. Comparative tests made at the beginning and end of the work day will show whether the worker has been overexposed; the sensitivity of the test is just below the U.S. recommended hygienic limit of CS_2 in air of 60 mg./m. The test becomes predictive of potential injury when comparative tests are made at the end of the work week and at the beginning of a new work week; hypersusceptible workers will not show a return to normal values at the beginning of the week. If exposure is continued, the test predicts that such workers will develop overt signs (polyneuritis) of CS_2 injury. The general pattern of response to overexposure to CS_2 is a steady decrease in E values throughout the work week. A normally reactive worker will return to normal E values, 8 or above, by the start of the new week. A hyperactive worker will not, but will start the work week showing only partial recovery in E values. It is these responders who will predictably show signs of CS_2 injury if exposure is continued.

Sufficient work claims to have been done on healthy nonexposed workers to show that diets usually high in sulfur, and disulfuram treatment for alcoholism, do not lead to false positive interpretations.

Comment

It is hoped that the description of the above tests will not merely call attention to the progress being made in our understanding and control of the hyper-

susceptible individual, but will stimulate wider adoption of these tests and encourage others to develop similar tests in the broad area of hereditary disposition to disease of industrial chemical origin. As our understanding of the relationship of disease manifestations to genetic abnormalities grows, a large part of our past bewilderment and surprise at finding workers claiming injury to health under conditions known to be protective will disappear. More than this, growing understanding of the underlying causes of hypersusceptibility will lead in many instances to measures for prevention and cure.

If this development succeeds, control of the worker's health will progressively become an individual matter; control will not be mainly the domain of the engineer, but will shift to the hands of the industrial physician.

(The references may be seen in the original article.)

EDITOR'S SECTION

FIFTEENTH ANNUAL ANESTHESIOLOGY REVIEW COURSE

Location: Wilford Hall U.S. Air Force Hospital, Lackland Air Force Base, San Antonio, Texas

Dates: 3 through 7 June 1968

This course is designed as a review for residents who have completed their training in Anesthesiology and desire to take the American Board of Anesthesiology Examination on or about 12 July 1968.

Requests should be forwarded in accordance with BUMED INSTRUCTION 1520.8 Series, immediately. A limited number of eligible officers may be provided with travel orders to attend at Navy expense. Others may be issued Authorization Orders by their Commanding Officer following confirmation by this Bureau.—Training Branch, BuMed.

FELLOWSHIP TRAINING IN GASTROENTEROLOGY

The Naval Hospital, National Naval Medical Center, Bethesda, Maryland, has recently established an approved program for Fellowship training in the subspecialty of Gastroenterology, directed by CAPT W. M. Lukash, MC USN. The one-year Fellowship will comprise training in the applied basic medical sciences, laboratory, and clinical, and the research aspects of Gastroenterology. The Fellows will perform fiber optic esophagoscopy, gastroscopy, and peritoneoscopy, gastrointestinal biopsies, and will conduct pancreatic function tests under supervision. Techniques and interpretation of gastrointestinal radiology will be covered by the Radiology Department staff of the hospital. The Fellow will participate in regular bedside teaching rounds, gastroenterologic consultations, and the scheduled Gastroenterology outpatient Clinic, and will be active in the hospital teaching program.

The trainee in Gastroenterology will be encouraged to attend sessions related to digestive disease, of the Medical Officers Course in Nuclear Medicine and Radioisotope Techniques given by the Naval Medical School. Instruction in diagnostic gastrointestinal parasitology will be given by the Department of Parasitology of the Naval Medical School. Eminent consultants from the University of Pennsylvania, George Washington University Medical School, and Johns Hopkins School of Medicine will assist in the training program.

Training will be given in pathology of the digestive tract at the Armed Forces Institute of Pathology. Scheduled clinical conferences and sessions on special diagnostic techniques will be held jointly with the Department of Gastroenterology, Walter Reed Army Hospital.

The Fellow may avail himself of seminars and lectures at the nearby National Institutes of Health, and of the resources of the National Library of Medicine, the world's largest research library in a single and professional field.

The Fellow will be encouraged to establish independent research investigation and also to participate in ongoing clinical research projects in the Gastroenterology Branch. Current projects are: 1. Evaluation of transaminase levels, post-activity, in patients convalescing from hepatitis; 2. Serum insulin levels in patients with chronic pancreatitis and the effect of secretin; and 3. Liver size correlated clinically with liver scans.

Prerequisite for acceptance is board eligibility in Internal Medicine. The number of available billets is limited. Applications should be submitted in accordance with BUMED INSTRUCTION 1520.10C prior to 1 July 1968 for training commencing July 69 to the Training Branch, Bureau of Medicine and Surgery.

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